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The Fruits of Conservatism

BY

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IN my early years as a gynaecological surgeon two cases occurred which profoundly affected my outlook. The first was that of a lady recently married who, wishing above all things to have a child, underwent subtotal hysterectomy on account of a single submucous fibroid. Being a woman of strong character and reticent fortitude, she accepted the blow without complaint, and, by assuming a proud indifference to children, held the insistent mother-instinct at bay, so that none but those who knew her well perceived the tragedy. I was amongst this number, and the pity of it is still keen in me to-day.

The second was that of a young girl, also recently married, from whom I removed both ovaries for bilateral dermoid cysts. Into the successful performance of the operation I put all my endeavour and all the knowledge and skill I then possessed, and I felt it grievously when on learning what I had done she conceived for me, as the instrument of her misfortune, a visible horror and undisguised aversion.

These two cases disturbed me greatly, for the practice followed was that universally carried out and taught at the time, and I asked myself whether in such instances the surgeon's knife must necessarily inflict a spiritual as well as a physical wound.

From that time I began to try, tentatively at first,[1] to do something better, and finding it possible, applied myself to a practice of conservatism, the fruits of which are embodied in this paper.

Conservation of the Uterus.

Abdominal myomectomy had been practised long before I began surgery, but on strictly selective lines, though in 1897–98 Alexander, of Liverpool, a pioneer before his time, had published three remarkable papers which made no impression on the current view.[2, 3, 4] Even till quite recently its textbook indications were given as solitary, or at most but few tumours, either pedunculated on the peritoneal surface, or if embedded in the uterus, then superficially so. Such conditions embrace only a small proportion of all cases of fibroids.

I set myself to make myomectomy so feasible, successful and safe as to render it a fair alternative to hysterectomy in every case, the decision which to perform resting solely on whether the woman's spiritual and bodily interests were best served by the one or the other. Excepting only in a very few instances in which special conditions exist I have succeeded, and now enter the operating theatre free of the trammels which at one time too often compelled my hand against my heart.[5, 6]

Mortality of Abdominal Myomectomy.

I have performed abdominal myomectomy 632 times, and have had seven deaths after the operation—a mortality rate of somewhat under 1.1 per cent. This figure is considerably lower than the average expert mortality rate for hysterectomy, as it appears in the recent and admirable paper by Arthur Gemmell.[7] Of the seven deaths, two were due to pulmonary embolism, but the remaining five were all occasioned by faults in technique which I have now corrected. Since the last of these deaths I have performed the operation 250 times without losing a patient. In assessing the significance of this result and also the further figures I am going to give, the scope of the operation as practised by me must be borne in mind. Neither size, position, nor number has been a deterrent. Of the 632 cases the tumour was solitary 254 times and multiple 378 times. The largest number of fibroids extirpated from a single uterus was 125, and on nine occasions I have removed numbers between 50 and 92.

New Fibroids.

In 1930 I sent a *questionnaire* to all the patients on whom I had performed myomectomy up to 1927. I had 210 answers, and on the information thus acquired I gave an Hunterian lecture on the subject.[8] I have recently sent a similar *questionnaire* to all my patients so operated on between 1927 and 1933, and have

had 169 replies, making 379 in all. Of these 379 patients new fibroids appeared nine times, or 2.3 per cent. Of these nine patients four had to undergo hysterectomy without having become pregnant in the interval between the operations, one had a child after the myomectomy and then underwent hysterectomy, one became pregnant after the myomectomy and had Caesarean hysterectomy, one had a second myomectomy with bilateral enucleation of ovarian cysts nine years after the first and four years later was delivered of a child by Caesarean section, while the remaining two have not required further operation.

In a certain proportion of the patients from whom I received answers to my *questionnaire*, the relative recency of the operation leaves time for new fibroids to appear in the future, but, making full allowance for this, the recurrence-rate should be under 4 per cent.

In all the instances in which new fibroids have formed the patient was exceptionally young at the time of the myomectomy. Reappearance is most unlikely in patients who, when operated on, are over 35 years of age, provided that the procedure is carried out thoroughly.

Menorrhagia.

Menorrhagia either persisted after the operation or appeared subsequently 12 times, or 3.1 per cent. Of these 12 patients six underwent hysterectomy (five with new fibroids), one was curetted, and two had mucous polypi removed, while in the remaining three the loss was kept in check by drugs.

Dysmenorrhoea.

One patient, subsequent to a myomectomy which it was hoped would cure her dysmenorrhoea, had to undergo hysterectomy on that account. In another also dysmenorrhoea persisted after the operation, but not to a degree necessitating further operation.

General Health.

Apart from these cases the *questionnaires* revealed in almost all the cases a most satisfactory improvement in health and an absence of genital symptoms. The actual number that so complained was under 2 per cent, including in this category a patient who subsequent to the myomectomy underwent a further operation for ovarian blood-cysts, and a second who developed a large cyst in the uterine wall. It was lined by cubical epithelium and was held to arise from a congenital "rest". Hysterectomy was performed.

Pregnancy.

Of the 379 patients concerning whom information was obtained there were 137 who, being married and within the child-bearing age, desired children. Of these 52 conceived after the operation, or 38 per cent. Natural delivery ensued 34 times, Caesarean section was performed 17 times, and there was one miscarriage.

These figures record only the pregnancies first occurring after the operation, but several of the patients have conceived twice and at least two of them three times.

It is noteworthy that my first sending out of a *questionnaire* elicited information that out of 77 women able and wishful to conceive after the operation 30 had actually done so. The percentage (39 per cent) was much higher than I expected, and I opined I had been lucky, but the second sending out elicited figures only slightly less good (22 out of 60), thus disposing finally of the myth that myomectomy usually leaves a uterus too deformed to conceive and bear a child in. The fact that only one miscarriage occurred to 51 full-time deliveries corroborates what we have already for a long time known, namely, that the reparative power of the uterine wall is remarkable.

The Operation and Age.

Concerning the application of the operation, I have in the past stated that, broadly speaking, myomectomy is the operation of choice in women under 41 years of age and hysterectomy on women over 41 years of age. Increased confidence in the results of myomectomy has led me of recent years to modify the latter part of this statement, for besides those not infrequent cases in which the patient, though getting on in years, resents the removal of her womb, there are others where the choice being left to the surgeon, myomectomy is properly chosen as the less severe operation of the two and equally certain to cure the symptoms. For example, menorrhagia in a woman of 46 years of age due to several fibroids in the anterior wall of an otherwise healthy uterus, is as surely cured by myomectomy as by hysterectomy, and in such an instance is not only the less severe of the two procedures, but leaves a suture line to which nothing worse than the bladder can adhere.

In short, I do not now observe any rigid rule with these older women but choose between myomectomy and hysterectomy according to which ever of the two promises to be the less severe undertaking.

Malignancy.

So far as I know no patient on whom I have performed myomectomy has subsequently developed malignant disease in the conserved uterus, but I once enucleated sarcomatous fibroids without realizing the metamorphosis. The patient was quite a young woman, and rapid peritoneal recurrence took place, of which she died. Cases like this require special guarding against. Sarcomatous fibroids have a peculiar hyaline appearance as a rule, and when this is observed the question of hysterectomy must be considered. If it is decided to carry on with the myomectomy the enucleated tumours should be microscopically examined as soon as possible after the operation.

Technique.

I have elsewhere very fully described the operative technique to which these results are owing.[9] Its essence consists in haemostasis during the operation by means of my myomectomy clamp, the placing of the suture line on the anterior wall of the uterus, deliberate and careful removal of the tumours so that not even a seedling is left behind, opening the uterine cavity to make certain there is nothing within it, removal of all redundant uterine wall before suturing is commenced, the avoidance of mattress sutures, and meticulous asepsis. When enucleating large tumours it is often best to remove them in bits (morcellation) as this is a much gentler proceeding than tearing and pulling them out *en masse*.

Conservation of the Ovaries.

Except in the case of malignant disease I hold it to be the clear duty of a surgeon to preserve the feminine sex-glands intact, or, if this is impossible, at least to leave in her body the full amount of undiseased ovarian tissue that she possesses.

The Ovarian Activities.

Fully functional adult ovarian tissue carries on four activities: (1) It promotes the sex sense, (2) it liberates fertilizable ova, (3) it controls menstruation, and (4) it stabilizes the nervous and neuro-vascular mechanism. As a woman gets older these four activities are discontinued, not simultaneously except in rare instances, but one by one and usually in the order in which I have set them down, but so long as one of them is maintained the ovarian tissue originating it cannot be said to be functionless. Moreover, in some women the ovarian tissue appears to be never more than partially functional, the first, second or third activity,

or the first and second activities, or the second and third activities, or the first and third activities, or the first, second and third activities being absent at all ages between adolescence and the climacteric. The fourth activity, whose cessation produces the symptoms and signs of the climacteric, is the most constant of the four, for it is never missing except in conjunction with or after the other three.

The only one of these four activities, the presence or absence of which can be decided with unvarying certainty, is that concerned with menstruation. The presence or absence of the ovular activity is usually inferred from the patient's age, but with no surety. For instance, at 50 years of age it would certainly be held to be absent, yet some years ago I saw a woman who conceived for the first time after she had passed her fiftieth birthday. The presence or absence of the activity concerned with the sex sense can only be judged of on information supplied by the woman herself and she may be unwilling to give it, or, giving it, may not tell the truth. There are undoubted instances of this activity persisting long beyond what is ordinarily considered the normal.

The presence or absence of the stabilizing activity can only be judged of negatively. If a woman has had climacteric symptoms it is certainly absent, but if she has never had them it must be presumed to exist. I have seen violent climacteric symptoms follow the removal of both ovaries in a woman over 60 years of age. There seems reason to believe, moreover, that the four ovarian activities are sometimes unequally distributed as between the two sides, and that apart from any evidence of disease or gross malformation. Certainly, as regards ovular activity it is not uncommon to find on one side an ovary containing follicles and corpora lutea in different phases, while in the other the ovary, though perfectly healthy, presents none of them. Every gynaecological surgeon of long experience has met with cases in which after the removal of one ovary only, the patient either never conceived again, lost her sex sense, ceased to menstruate, or had climacteric symptoms.

These considerations show that, except in malignancy, the surgeon should strive to preserve in the patient's body every atom of undiseased ovarian tissue.

The Ovaries in Hysterectomy.

When I began gynaecology this view was not held, and removal of both ovaries was commonly carried out on the

slightest grounds and frequently for operative convenience only.* One would have thought that to-day such heathen practice would be long since dead and buried, but its wraith lingers yet in quite recent papers and discussions on whether, when performing hysterectomy for nonmalignant conditions, the ovaries should or should not be removed as well. Those who still maintain the practice of removing them justify it on the grounds that ovaries left behind may become diseased. The argument has never appealed to me, and indeed one could justify almost any operative extravagance by it. The number of times I have had to operate on ovaries conserved at a hysterectomy can be counted on the fingers of one hand, and my experience is long and large. It is also said that ovaries so conserved cease to be active in a very short time. This, again, is the reverse of my experience. I have had many opportunities of seeing ovaries through an abdominal incision at various periods after hysterectomy, and they appear perfectly normal. I think it is forgotten that the majority of hysterectomies are carried out on women over 40 years of age whose normal climacteric is not more than eight to ten years distant.

The Ovaries and Radiological Treatment.

Forty years ago the removal of both normal ovaries for the arrest of menorrhagia was a common operation. The radiological measures carried out to-day for the same purpose are on a par with it, for though the patient escapes the drawbacks of an abdominal operation the end result, namely, the destruction of ovarian function, is the same. The old surgeons could at least excuse the misfortune they inflicted on the grounds that hysterectomy was at that time a dangerous operation. There are certain cases of women approaching the climacteric in which radiological treatment is to be approved, though even of such I have seen not a few who bitterly regretted it, but to resort to it in women still in the thirties is to me senseless and cruel.

The Ovary and the Appendix.

It is a common practice amongst surgeons of imperfect training and small experience to remove the right ovary in the course of

* I have often seen an ovary removed in the course of hysterectomy for fibroids because it was sessile on the enlarged body of the uterus. There is no necessity to do this if a ring forceps be temporarily placed on the ovario-pelvic ligament to control the blood-flow from the proximal end of the ovarian artery during the separation of the ovary from the uterus.

an appendix operation "because it had a cyst upon it". It is only the ovary accessible through an appendix incision that is so commonly said to be afflicted with this cyst, but the suggestion is strong that had Nature placed the appendix on the left side the left ovary and not the right would be the one sacrificed by the hedge-surgeon* who performs the operation. An ovary with a small cyst on it should not be removed. If the cyst is a normal follicle on the point of bursting it should be left alone. If it is a real pathological formation it should be enucleated.

Enucleation of Ovarian Tumours.

This leads me to the conservative treatment of ovaries enlarged by cyst formation. I showed many years ago that many types of ovarian cysts are enucleatable from the ovary. In this category are included dermoid cysts, follicular cysts, ovarian blood-cysts (chocolate cysts), whether derived from the follicle or the corpus luteum, as well as certain fibromata and rarer solid formations such as granulosa tumours. Most multilocular pseudomucinous cysts are so large by the time they are operated on that enucleation is impossible, but when small they also can be treated so.

The advantage of enucleation over the attempt to leave a part of the ovary unaffected by the cyst is that such an unaffected part is often not obviously present, whereas enucleation conserves the entire ovarian substance, much stretched, of course, but capable of being restored by sutures to a reasonably normal shape.

It should be taken as an axiom that a woman having ovarian cysts who continues to menstruate has within her some portion of healthy functional ovarian tissue, and except when the cyst is malignant it is the surgeon's duty to conserve that portion. I have no opinion of ovarian grafting. Healthy functional ovarian tissue should be conserved in its natural situation.

The Results of the Operation.

In the last 15 years I have performed conservative operations (mostly enucleation) for ovarian cysts and tumours 120 times. Of these 120 patients 58 had blood (chocolate) cysts, 31 on one side only and 27 on both sides. There were 40 cases of unilocular serous cysts, 26 being unilateral and 14 bilateral.

* "Hedge-surgeon", an analogue of the hedge-priest referred to by Sir Walter Scott. See the notes to "Ivanhoe".

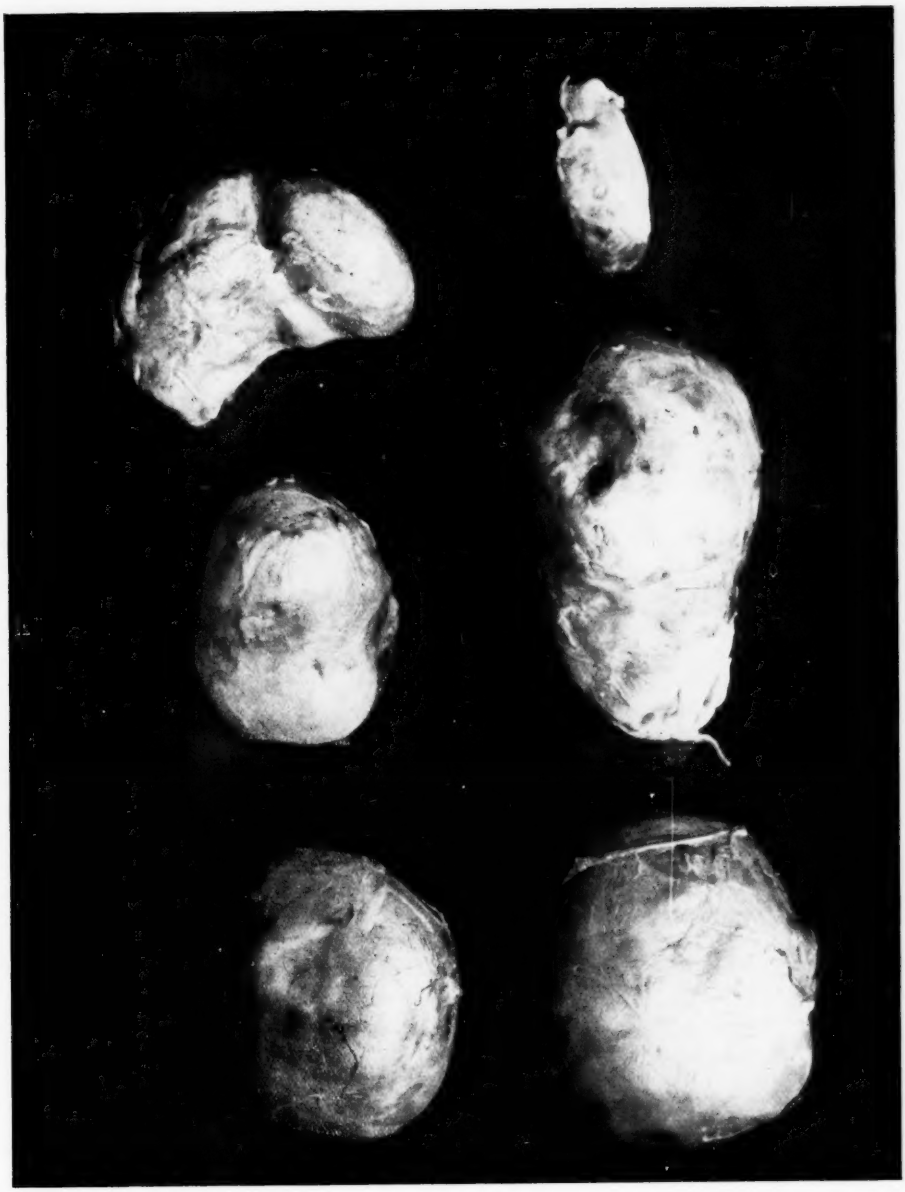

FIG. 1. SIX DERMOID CYSTS.

Three enucleated from the right ovary, and three enucleated from the left ovary (½ natural size).

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There were four patients who had a blood-cyst on one side and a unilocular serous cyst on the other. There were 11 cases of dermoid cysts, the cysts being unilateral in seven cases and bilateral in four. In one case the dermoid on one side was complicated by a blood-cyst on the other. Multiple dermoids in an ovary occurred four times. One patient had two in one ovary, two patients had three in one ovary and two in the other ovary, and one patient had three in both ovaries.

Besides these there were three patients with multilocular cyst adenomata, three patients with solid granulosa tumours, and one patient who had three fibromata on one side and two on the other.

Mortality.

There have not been any operative deaths in this series.

Pregnancy After the Operation.

I sent out a *questionnaire* to all these patients except those operated on less than three years ago, and have had 90 replies. Of this number 16 have conceived since their operation, 32 have not conceived though they were married, of child-bearing age, and wanted to have children, and 42 have not conceived, being either beyond the child-bearing age or not wishful to do so.

Of the pregnancies, five occurred after the enucleation of blood-cysts, and in two cases the enucleation was bilateral. Six occurred after the enucleation of serous cysts which in two cases were bilateral. Four occurred after the enucleation of dermoid cysts which in two cases were bilateral, and from one of these women I had removed three dermoids from one ovary and two from the other. The most interesting pregnancy is the last, for it occurred after the enucleation of a granulosa tumour from one ovary. Included among the group of patients who replied to my letter is the second case in which I removed three dermoids from one side and two dermoids from the other. She does not, unfortunately, want to conceive though she is of an age to do so. This year I have had another patient from whom I enucleated six dermoids, three from either side. She was six weeks pregnant at the time and is now getting near term. The conjoined masses formed a swelling which came above the umbilicus. (Fig. 1.)

Recurrent Disease.

The general health of all the patients on whose ovaries I have performed a conservative operation and who replied to my

letter has been excellent, except in four instances, all of whom had had blood-cysts enucleated. Of these one developed new cysts and was operated on by another surgeon and died of sepsis. The remaining three all developed uterine endometriosis and had to undergo hysterectomy.

Certain gynaecologists adopt a drastic course when dealing with cases of ovarian blood-cysts (chocolate cysts), removing one or both ovaries and not infrequently the uterus as well. It will be seen that I have adopted the opposite course. Those who advocate drastic measures hold that endometriosis may develop into malignancy. In cases of ovarian endometriosis more or less irremovable thickening of the posterior pelvic peritoneum has as a rule to be necessarily left behind whatever operation is performed, and if there be any substance in the allegation this would remain a basis for malignancy to start upon. But such supervention must be very rare for I have never seen it. In my experience this thickening disappears after several years, and in the meantime does not cause any symptoms. The cysts may recur undoubtedly, but the one case I here record is the only example I know of. The apostles of stringency would be on firmer ground if they advocated hysterectomy to prevent subsequent uterine endometriosis, for my figures show that this occurs after enucleation in rather under 6 per cent of the cases. But is it worth sacrificing the uterus and the chance of pregnancy for this small risk? I think not, especially in view of the fact that I have five cases of pregnancy to set against the three cases of subsequent hysterectomy.

Reparative Operations on the Fallopian Tubes.

Since 1921 I have performed 70 reparative operations on patients having double tubal closure. There have not been any deaths. The operations performed have been as follows: Salpingostomy, forty-four times; freeing tubal kinks, seven times; tubal exsection and anastomosis, two times; reimplantation of the tubes into the uterus, nine times; reimplantation on one side and salpingostomy on the other, three times; double reimplantation with double salpingostomy, four times; and making an ostium in the uterine cornu of a patient who had had both tubes removed, once.

Pregnancy After the Operation.

I sent out a *questionnaire* to all these patients except those operated on less than two years ago and received 37 replies.

Among these 37 women there were seven who had conceived. My percentage of successes (18 per cent) is, therefore, greater than that recorded in the recent and valuable paper by Bethel Solomons, the figure there being 15 per cent for a number of collected cases.[10] My numbers, however, are small, and I may have been fortunate, but the gratifying point is that I have had successes after several of the different types of operation and not merely after salpingostomy. The distribution of these successes is as follows: After salpingostomy, twice; after reimplantation, twice; after reimplantation on one side and salpingostomy on the other side, once; after double reimplantation with double salpingostomy, once; after tubal exsection and anastomosis, once.

It is held by some authorities that the operation of reimplanting the Fallopian tubes into the uterus is so unlikely to achieve the desired result as not to be worth doing. My results show that this is not the case.

Of the two pregnancies that followed reimplantation, one was in the Fallopian tube reimplanted, which by great misfortune was the only one capable of being repaired. I had to remove the pregnant tube.

The rule I have followed is not to operate unless the semen has been proved active and the Fallopian tubes have been found to be blocked on two occasions separated by a three months' interval, unless at the first testing a thickening or tumour can be felt.

I explain to the patient that on opening the abdomen I may not be able to effect the object of the operation, and that supposing I am able it does not by any means follow that she will become pregnant. She must, in short, be prepared to take the chance of a chance.

Conclusion.

Although as compared with the opening years of this century there has been some advance, it is certain that, except in a few quarters, conservatism to the full extent of its possibilities, though many do it lip-service, is not practised by gynaecological surgeons in this or any other country, while amongst surgeons who only operate occasionally on the female organs, the lack of exemplars causes it to be practised still less. I am impatient for a change of attitude.

Timidity in abandoning courses proved at least to ensure physical recovery, though purchased at possible psychological cost, the fetters welded by teachers on the imaginations of the taught, and the docile sinking of individual outlook in the mass-view of a school; it is these that maintain the older, harsher methods. I have shown that they can be replaced by an equally safe conservatism, which is not only much more beneficent, but bespeaks that compassionate artistry of mind, unguided by which, surgery is scarcely worthy of being reckoned amongst the arts.

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Dysmenorrhoea : The Oldest Theories and the Newest Treatment.

BY

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> Pain is the most important of complaints and the commonest and most clamant symptom with which the physician has to deal. It drives the patient to his doctor, whose most urgent task is often its relief, while the search for its cause provides some of the most difficult problems he has to face on the clinical side. Volumes have been written about it. There is hardly a single number of the recent issue of the *Journal of the American Medical Association* in which there is not a reference to some aspect of the subject. Interest in pain is not confined to the medical world. Philosophers have pondered over it, and the problem of pain has raised issues of deep significance in metaphysics and theology.—WATERSON.[1]

So much stress has been laid upon the personal and variable character of pain, its similarity to feelings and, like the latter, its unreliability as a guide to the state of the living organism, that it is regarded by many as a purely mental and not a physical or quasi-physical reality. If this view is correct, it follows that pain cannot be explained in terms of physical categories. Our knowledge of the physical world, for example, and the physiological concomitants of knowledge such as feeling, emotion, and presumably pain, cannot be explained in terms of lower categories without destroying the validity of knowledge and the significance of the mind's emotional reactions. It also follows that the physical theories of dysmenorrhoea, the special type of pain with which this paper is concerned, fall to pieces like Alice in Wonderland's house of cards. We shall have to examine, then, very closely the arguments on which the purely psychogenic theory of pain is based.

The main argument is that feeling, emotion and pain are a triad of psychological impressions produced by the world of matter in which the latter is seen "as in a glass darkly". This argument is a corollary of Locke's theory of representative perception or psycho-physical parallelism. According to Locke,

not only feeling, emotion, and pain, but all the so-called secondary or imponderable qualities of matter such as sound, colour, scent, etc., are impressions made upon the percipient mind by the physical or quantitative world which is inferred from these mediating experiences. For these symbols, it requires us to substitute, as our sole guide to the world of physical fact, inferences from impressions which are regarded as the passing effects of causes which, by hypothesis, are never themselves perceived. Surely the shadowy procession in Plato's cave would provide a surer guide than these to truths which lie beyond the limits of immediate experience.

According to the theory of psycho-physical parallelism, then, so-called organic pain is merely symbolic of certain gross pathological conditions of the organism and is, therefore, an uncertain guide to the nature of such conditions. So-called functional pain is due to a neurosis or psychoneurosis, whatever that may mean from the point of view of psycho-physical parallelism.

It is no matter for surprise, then, that recent years have witnessed the introduction of a host of objective methods of studying disease such as the radiological examination of the alimentary tract, cholecystography, etc., and that the clinical study of pain has suffered a simultaneous eclipse.

According to the orthodox theory of immediate perception, provided our sense organs, which condition the secondary qualities of matter, and the spatial and physical conditions of the medium between the object and these organs are normal, glorious symphonies, autumnal woods, gleams of sunshine on misty crags, and all the rest of Nature's pageant, are as much a part of the physical universe as the colourless mathematical qualities of matter. The advocates of the purely psychogenic theory of pain must rest their case, then, on surer foundations than those provided by the Lockeian view of knowledge. This theory, which leads to subjective idealism in philosophy, is accepted by many medical men, physiologists in particular, who do not realize the insecure foundations on which it rests and the logical implications of the theory.

On what positive grounds do we assume that pain is a physical or quasi-physical reality? In the first place, pain, like other physical qualities, is appreciated through the medium of a sensory apparatus, the anatomy of which, I admit, is imperfectly understood. Mental phenomena are inspected without such a medium. In other words, they are introspected. Secondly, pain

has the material character of spread-out-ness and can be localized in space. Somatic and so-called referred pain, for example, can be localized as accurately as colour and sound, which are regarded as physical qualities, except by the advocates of the theory of representative perception. Mental phenomena, such as feeling and emotion, have no such spatial and local characteristics. Lastly, the category of physical causality is applicable to pain, but not to purely mental phenomena such as feeling and emotion. When we receive the wireless message: "Will John Smith of such-and-such an address go to the London Hospital where his mother is seriously ill," we understand the feelings of John Smith, but we may not share them. Our feelings, in other words, do not depend upon the physical stimulus as such, but upon the *meaning* which it conveys to our intelligence.

Pain is not a quality of inorganic matter. We have no reason to believe that plants suffer pain. It is peculiar to sensitive organisms. It is not, therefore, purely physical. It is a quasi-physical or psycho-physical reality. Pain and other psycho-physical and intra-organic realities such as hunger, thirst, etc., are called in the jargon of modern philosophy tertiary qualities of matter in order to distinguish them from the secondary, and from the primary, qualities, which, though conditioned by the organs of sense, are extra-organic.

Hallucinations of sense being psycho-physical realities are also included among tertiary phenomena. Hallucinations which are mistaken by the subject for extra-organic realities are called imaginary objects. There can be no such thing as an imaginary pain; for, although it may sometimes be localized outside the body, such as the pain which not infrequently follows the amputation of a limb, it can never be mistaken for an extra-organic reality.

Pain, being a quasi-physical reality—and this is a point of vital importance—obeys the laws of physical causality. On the other hand, the purely spiritual qualities of mind such as knowing, feeling, and willing are conditioned but not determined by physical causes.

A critical analysis of psycho-physical parallelism on which the purely psychogenic theory of pain is based is indispensable to a proper understanding of the genesis of the traditional theories of dysmenorrhoea, the validity of which it is the special purpose of this paper to discuss.

As a reaction against the purely psychogenic nature of pain, there has been considerable interest of late in the clinical study

of this reality with a view to a better understanding of the physical causes which provoke it. The precise mechanism of visceral colic, of which dysmenorrhoea is a classical example, has been the subject of much research within recent years. In order to understand its mechanism, careful analysis must reveal not only the place and time of its occurrence, but also the intensity and quality of the pain so far as it is humanly possible to do so. In an earlier paper[2] I stated:

"Pain is so variable in intensity and quality that a precise definition is not always an easy matter. We have no choice, then, but to place our dependence upon the statement of each individual and, as we do so, we register one of the weakest points in our system of clinical investigation. After long and careful analysis, I think we have at last succeeded in separating out the characteristic features of genuine dysmenorrhoea. The pain is characteristically intra-menstrual, although, at times, it may be pre-menstrual as well. It is essentially spasmodic or tetanic in character, but never a dull ache. Occasionally it is accompanied by painful spasms in the bladder and the rectum. Dysmenorrhoea, in the sense defined, must be carefully distinguished, on the one hand, from the dull aching pain of menorrhalgia which is, characteristically, pre-menstrual in time and relieved by the menstrual flow, and, on the other hand, from anxiety and hysterical manifestations which sometimes accompany an almost painless menstruation.

"It is generally agreed that undue muscular contractions constitute the appropriate stimulus to the production of spasmodic visceral pain. Whatever, then, be the fundamental cause or causes of dysmenorrhoea, the nature of the pain would suggest that the proximal or immediate cause is a spasmodic or disordered contractility of the uterine musculature. If this view is accepted, it is obvious that the fundamental cause or causes of dysmenorrhoea can only be discovered in the light of the factors which govern the reactivity of the uterine muscle which to-day is regarded as an essential part of the menstrual process."

In the light of these observations, I then proceeded to review the modern theories in regard to the fundamental aetiology of dysmenorrhoea. Novak's theory, which received honourable mention in my paper, has not been mentioned in a single text-book of gynaecology with which I am familiar. The recent edition of Eden and Lockyer is the only textbook in the English language which refers to Whitehouse's theory, which I also elaborated upon in my paper. It is significant that Whitehouse

himself is the editor. Several textbooks refer to a primary disturbance of the abdomino-pelvic autonomic system as a possible cause of dysmenorrhoea. They do not, however, indicate the type of dysmenorrhoea to which this theory is applicable; whether it is the sympathetic or parasympathetic system which is at fault, or the mechanism of the production of the pain of dysmenorrhoea due to the sympathetic-parasympathetic imbalance. My paper was in the main an attempt to answer these questions in the light of a critical analysis of the reflex disturbances of the bladder and rectum which accompany the special type of dysmenorrhoea to which the theory is applicable. The views expressed in our gynaecological textbooks in regard to the aetiology of dysmenorrhoea are, in short, a tiresome repetition of traditional views which are copied from one textbook to another without, as we shall see, any stronger arguments to support them than the mere *ipse dixit* of the particular author.

Traditional Theories of Dysmenorrhoea.

In discussing a paper on "Intrinsic Dysmenorrhoea", read by Blair-Bell[3] at the Congress of Obstetrics and Gynaecology held in Edinburgh in 1923, Fairbairn[4] said: "That he would like to divide the medical attitude towards a disturbed function such as dysmenorrhoea into two extremes; those who always found kinks and twists and other mechanical deviations to explain it and cured it by operating on what they found, and those who referred the same disordered function to a repressed instinct, usually sexual or reproductive, and treated it by psychoanalysis or something of that sort. In between these extreme cases came the ordinary folk swinging to one side or the other as their fancy took them. The reader of this paper he should put on the kinkological side; he would put himself a little on the psychological side, especially in regard to treatment."

It is not difficult to trace the influence of the theory of psychophysical parallelism on the traditional views of dysmenorrhoea, so admirably expressed by Fairbairn. However ill-fitted it may have been to survive serious criticism, the theory of representative perception or psycho-physical parallelism had merits which it would be unkind to forget. Its realistic side appealed to the extreme or naïve realists; for it left standing the quantitative or mechanical world of matter which they had no intellectual scruple in regarding as the parent of mental phenomena, including the secondary and tertiary qualities of matter. The theory

also appealed to the idealists who insisted upon a spiritual pedigree for the secondary and tertiary qualities which, from the point of view of representative perception, are included among the phenomena of mind. There was thus something for everybody except the orthodox or moderate realists who were not satisfied that the tertiary, secondary and even, as we shall see later, the primary qualities of matter could find honourable accommodation in the framework of two mutually independent worlds, viz., the world of matter, on the one hand, and the world of minds on the other.

Now dysmenorrhoeic pain, which is a tertiary quality of matter in the sense which I have defined, is either organic or functional. If it is organic, then, from the point of psycho-physical parallelism, it symbolizes some gross mechanical condition of the organism. If it is functional, then it can only be due to a pyschogenic cause; for the theory of psycho-physical parallelism does not admit of a *tertium quid*.

The protagonists of psycho-physical parallelism are moved to one alternative or the other according as their tastes are either materialistic or spiritualistic. In the language of Fairbairn, they swing to either the kinkological or psychological side as their fancy takes them.

The Theory of Mechanical Obstruction.

One of the oldest theories, which is still quite widely held, is that dysmenorrhoea is due to obstruction to the outflow of menstrual blood on account of acute anteflexion of the uterus. Many arguments can be advanced against the theory of mechanical obstruction. Anteflexion is often observed in the absence of dysmenorrhoea, while, on the other hand, the most severe examples of menstrual pain may occur in women whose uteri are not anteflexed. It was observed by Novak[7] that at the acme of menstrual pain a probe could be easily passed into the uterine canal, without any evidence of obstruction of any kind. It has been computed that the rate of discharge of menstrual blood in the normal averages only two-thirds of a drop per minute. "It is difficult," says Novak, "to believe that anteflexion could produce sufficient obstruction to interfere with the exit of such small amounts . . . that is not to say that genuine obstructive dysmenorrhoea may not occur occasionally from such a cause as a ball-valve polypus, or a fibroid that may, perhaps, choke the uterine or cervical canal."

The Developmental Theory.

With the lessened credence in the obstructive theory, the view has been steadily growing that hypoplasia, a condition more fundamental than anteflexion and other congenital anomalies—a condition of which they are perhaps the expression—is the *fons et origo mali*.

Even when the uterus is markedly hypoplastic, as in the so-called pubescent uterus, dysmenorrhoea may be absent, while, on the other hand, we frequently observe excruciating pain when the uterus is of normal size. Besides, there is no evidence that anteflexion is an indication of a hypoplastic uterus, for the uterus may be of normal size even though acutely anteflexed. The chief evidence against the developmental theory of dysmenorrhoea lies in the fact that primary dysmenorrhoea is often an acquired disturbance. In many cases menstrual pain may not make its appearance until long after puberty. Such a history was noted in nearly one half of the last hundred cases observed by Novak.

It seems to me that, at the Edinburgh meeting, the reader of the paper, and many of those who took part in the discussion, stressed unduly the importance of kinks and congenital anomalies as the basic factors in the production of genuine dysmenorrhoea. Eden's philosophic remarks raised the discussion to a higher plane of thought. "Until Eden came forward", says Fairbairn,[4] "every speaker concentrated on local conditions and never got beyond them."

"We ought to take the widest possible view", said Eden, "and it was especially important in dealing with dysmenorrhoea to understand what the menstrual process implied. There was the part played by the uterus. There was the part played by the ovaries. There was the part, very much undermined at the present time, played by other endocrine glands, and, lastly, there was the part played by the nervous system. Any one of these factors might conceivably become a cause of pain."

It was this significant statement which prompted the writer to a revision of the meaning and aetiology of dysmenorrhoea in the light of the factors which govern menstrual bleeding and the expulsion of the menstrual decidua.

Psychogenic and Constitutional Factors.

According to Menge,[5] the physiological menstrual contraction waves of the uterus which are unnoticed by normal women are felt as labour pains by women who are psychoneurotic. This

theory is a direct negation of the view that undue or irregular muscular contractions of the uterus are the immediate or proximate cause of dysmenorrhoea. This version of the psychogenic theory rests mainly upon the false theory of psycho-physical parallelism dealt with in my introductory remarks.

Another reason for the psychogenic theory as expressed by Menge is the failure to recognize the necessity of a definte nervous apparatus for the production of pain. Many people entertain the idea that pain is merely a manifestation of some sort of increased or disordered activity of any sensory nerve; that, in other words, every kind of pain, including dysmenorrhoea, can arise in consciousness independently of the afferent impulses which are its ordinary cause. Recent work on sensory physiology has completely shattered this view. It has been shown that variations in the stimulus applied to afferent nerves increase or diminish the intensity of the sensation, without change in its quality. Division of the optic nerve may excite some visual sensation, but it does not cause pain. Pain, therefore, whether somatic or visceral, has its own sensory apparatus, and its appropriate physical stimulus.

It is a common experience, of course, that the intensity of pain may be diminished or increased by psychogenic factors. If objects which provoke excitement, anger, or pleasure, occupy the field of consciousness the threshold for pain becomes temporarily raised. The soldier may be hardly aware he is hit until he sees blood flowing from his wound. On the other hand, introspection, anxiety, neurosis and morbid attention will augment the effects of painful stimuli. Dysmenorrhoea, therefore, may be aggravated by psychogenic causes. We have yet to prove, however, that it is attributable to such causes. We might add, in passing, that constitutional factors also increase the intensity of pain. Dysmenorrhoea in women whose constitution is below par can often be rendered tolerable by building up the general health and insistence upon general hygiene.

What proof, if any, have we that undue or irregular uterine contractions which we regard as the appropriate stimulus to the production of dysmenorrhoea can be provoked by psychogenic factors? In order to give a confident reply to this question, it is necessary to face the difficult problem of the relation between mind and body.

According to the theory of psycho-physical parallelism or representative perception, which is a logical development of the Cartesian dualism of mind and body, all mental phenomena,

whatever their character, are the result of physical causes, while physical events are never the result of mental causes. Mind may know matter, but it cannot move it. Matter produces mind, but cannot know it. From the point of view, therefore, of psycho-physical parallelism or epiphenomalism, as this type of mind-body relation is sometimes called, a disturbance of normal uterine contractions by mental causes is an impossibility. It is an unshakable conviction, however, of every one of us, at least in his unphilosophic moments, that he can, of his own free will, lift his arm, use his legs, and cultivate his garden. News of the death of a dear friend upsets his digestion. If these are miraculous acts, from the point of view of epiphenomalism, it would seem to follow not merely that miracles are of constant occurrence, but that man's main occupation is to perform them!

The theory of epiphenomalism may be legitimately accepted as a working hypothesis by physiologists so long as they regard the physical world, including our own bodies, as a self-contained system in which dynamic and mechanical laws alone operate. When we seek to inquire, however, how we come to valid knowledge of the material universe and how its course can be modified by human intervention, the theory completely breaks down.

Epiphenomalism must be distinguished from the theory of pre-established harmony of the extreme form of psycho-physical parallelism. According to the latter theory, mind and matter are regarded as self-contained systems which develop along parallel lines without any influence upon each other. The theory is purely speculative and serves the interests neither of physiology nor psychology.

Aristotle's Theory of Hylomorphism.

According to Aristotle, the human organism is something more profound than a mere casual or accidental relation between two independent and incompatible substances, viz., body and mind, which is the Cartesian view. It is an organic synthesis of two fundamental but incomplete substances, viz., primal matter, *hule*, and substantial form, *morphe*, which are complementary to each other. The matter is the raw material out of which the organism is evolved. In itself, it is indeterminate and can only exist in organic union with the form. The latter is that which gives the human organism its characteristic features. It exists potentially in the primal matter, and under the influence of the external and internal environment of the organism it

becomes progressively realized. The form, therefore, is the alpha and omega of the human organism. At the level of biological and instinctive behaviour the substantial form or soul is, in the language of Aristotle, completely 'immersed' in matter. The organism is blindly and inevitably directed towards its end or the realization of its form by the inevitable laws of physiology. At the level of human experience or organized knowledge, the substantial form or mind, as it is called at this level, becomes conscious of the end of the organism's activities. That is to say, it becomes self-conscious. Therefore it transcends, but does not annul, the laws of physiology, for it still needs (in this world at any rate) the mechanisms of the organism in order to accomplish its purposes. It is enabled, however, within certain limits, to select those mechanisms which are relevant to its purposes. In short, at the level of human knowledge, man becomes a free agent. In the interests of economy, of course, the mind delegates to mere mechanism the execution of many purposes which are carried out blindly and inevitably. At any moment, however, the mind, in the interests of the organism, may interrupt the uniformity of human behaviour.

Whether our interests are theoretical or practical (and the interests of physicians are both), Aristotle's theory is the only theory which does not lead either to barren scepticism or arrogant dogmatism, on the speculative side, or to hopeless fatalism or unlicensed liberty, on the practical side.

Everyone admits that the tertiary qualities of matter, e.g., pain, hunger, etc., are intimately associated with our organisms which we carry with us wherever we go. Even the protagonists of the psychogenic theory of pain admit that it is conditioned, if not determined, by the laws of sensory physiology. Hallucinations of our special sense organs demonstrate clearly the relativity of the secondary qualities of matter, such as sound, colour, etc., to these organs. In spite of the fact that the apparent shape and size of a material body depend upon the particular standpoint of the observer, few of us realize that even the primary qualities such as size, shape, velocity, etc., which belong to the quantitative world of matter, are also conditioned, in a very special manner, by the organs of sense. The relativity of the primary qualities to our organisms which finds its fruitful application in the modern theories of gravitation and the space-time continuum was just as familiar to Aristotle and St. Thomas Aquinas as it is to Einstein.

Only, then, through the medium of our sense organs and

within the limits imposed by these organs are we enabled through the special body-mind relation formulated by Aristotle, to have direct intellectual commerce with the material world. Only on such conditions are we enabled to bend this world to our special purpose.

As a matter of special interest to practising physicians, Aristotle's theory is the only theory which can reconcile the differences between the antagonists and the protagonists of psycho-therapy; for it is compatible with the view that functional disease, of which dysmenorrhoea is one of the clearest examples, can be explained either on a physiological or psychological basis.

According to Aristotle's theory, which has lost nothing of its strength and appeal with the passage of years (for is not the renaissance of the philosophy of the present century a rediscovery of Aristotle's principles?) there is nothing miraculous in the influence upon body or for that matter upon the extra-organic world. Its influence upon the latter, however, is restricted by the amount of knowledge which our sense-organs admit to the perceiver. Its influence upon the former is restricted *within the limits* imposed by the organism. That influence must be understood, however, in a teleological, not in a mechanical or physical, sense. According to Aristotle's theory there can be no conflict between teleological and mechanical categories because there is really no contact between them. They move as it were on different planes of thought.

As we do not know the purposes of the organism at the biological and instinctive level, we have to depend entirely upon physiological mechanism in order to account for the behaviour of the organism at this level. At the level of human knowledge, however, we become conscious of the purposes of our own organisms and these purposes are revealed to others through the medium of a common language. Therefore, at the level of human knowledge, psychological categories transcend but do not annul the physiological categories, for we still require to know the mechanism which we employ in order to realize our purposes. Sensory physiology teaches us that our voluntary activities are expressed through the medium of the somatic nerves and muscles. Our emotions and feelings, which are theoretically controllable and which play such a vital part in the development of the psychoneuroses, are subserved by the sympathetic and involuntary muscular systems.

Elsewhere,[2] I have pointed out that dysmenorrhoea, which is

accompanied by reflex disturbances of the bladder and rectum, is due to spasm of the cervical sphincter, the result of a disturbance of the abdomino-pelvic sympathetic system. We have prepared the ground, therefore, for the reception of the view that this type of dysmenorrhoea may be fundamentally due to psychogenic causes. Have we any direct proof, however, of such a causal relation?

In a previous communication[6] I referred to a case in which dysmenorrhoea accompanied by cystalgia and rectal spasm was associated with marked symptoms of anxiety neurosis which, according to the patient, ante-dated the pain. The chronological order of the sequence of events is suggestive but not conclusive of a causal relation. The relief of menstrual pain and the other pelvic discomforts by psychotherapy would have established beyond doubt a causal relation. As the severity of the pain demanded the speediest and most certain method of treatment, resection of the presacral nerve was carried out instead. No definnite conclusion, therefore, can be drawn from the case.

As a protest against the theories of twists and congenital anomalies, some gynaecologists, notably J. Novak,[7] believe that all cases of dysmenorrhoea are attributable to psychogenic factors. Now the majority of cases of dysmenorrhoea, as we have seen elsewhere,[2] are due to a disturbance of the local mechanism which controls the spontaneous movements of the uterus. Whether the mechanism is myogenic or neurogenic is immaterial. Now this disturbance can be satisfactorily explained on the basis of an imbalance in the ovarian hormones which control the movements of the uterus. It is only the relatively few cases of dysmenorrhoea due to disturbance of the autonomic nervous system which are theoretically explicable on a purely psychogenic basis.

We are willing to admit, then, that psychogenic factors may augment the intensity of dysmenorrhoeic pain which reaches the brain along the afferent fibres of the superior hypogastric plexus. We also believe that there is an antecedent probability that psychogenic causes may disturb the normal contractions of the uterus through the medium of the efferent fibres of the hypogastric plexus. We have no direct evidence, however, of a causal relation.

Pseudo-dysmenorrhoea.

At the beginning of this paper, I distinguished between genuine dysmenorrhoea, which is a functional pain, and menor-

rhalgia, which is a symptom of some gross pelvic condition which may not always be clinically recognized. In the past there was a certain amount of confusion between these two conditions. To-day menorrhalgia is almost universally recognized as distinct from dysmenorrhoea and will not detain us any longer. In certain women there occur at the periods anxiety and hysterical symptoms, sometimes very alarming, which may easily be mistaken as a measure of the severity of the periods. It is true, of course, that very severe pain such as gall-stone colic and even genuine dysmenorrhoea may be accompanied by fear and other psychological concomitants. On the other hand, severe anxiety and hysterical manifestations may usher in an almost painless menstruation. Some years ago I was asked to see a girl with hysterical aphonia and semi-stupor which dated from a normal period and continued for 10 days. During a fishing holiday in the West of Ireland, I saw, in consultation with the local doctor, a girl who, on the first day of a normal menstruation, had a marked gastric fixation which might have easily been mistaken for a perforated duodenal ulcer. These nerve storms are probably the result of some past sexual experience which has been repressed or forgotten. On account of some subtle association between the menstrual flow and the original experience, the former provokes the same emotional reactions as the latter—a beautiful example of what is known in sensory physiology as the conditioned reflex. Whatever be the psychological explanation, such cases imperatively demand psychological analysis and psychotherapeutic treatment.

Treatment of Dysmenorrhoea

Whatever be the fundamental cause or causes of dysmenorrhoea, if we accept the view that the immediate cause is a disordered contractility of the uterine muscle, we should expect that, on account of their quiescent effect upon that muscle, the hormone of the corpus luteum and the anterior-pituitary-like hormone from the urine of pregnant women should relieve the pain. The corpus luteum hormone which is available for therapeutic purposes is very disappointing in its results. The more active extracts which have been used for experimental purposes are almost impossible to obtain in sufficient strength and the prices are prohibitive in these islands, at any rate. In a recent number of the *American Journal of Obstetrics and Gynecology*,[8] there is a record of remarkably good results obtained by an

active extract of the corpus luteum supplied by the Schering Corporation under the name of progesterone. Seventeen cases of genuine dysmenorrhoea were treated with remarkably small doses of this hormone. Three to 25 ruthenium British units were administered from three to six days before the menstrual flow or before the onset of pain. Forty-seven per cent obtained complete relief, 11.7 per cent claimed partial relief, and 41.3 per cent received no relief. According to the investigators, C. A. Elden and K. M. Wilson, the failures were probably due to either too late or too early administration of the hormone. "Continued application," they say, "of this hormone under controlled conditions will eventually bring to light a better understanding of its use."

W. P. Kennedy (cit. Eden)[9] has published the results of 50 cases of dysmenorrhoea treated by means of oestrin or folliculin. The results are as follows: Completely cured, 10; improved, 30; very much improved, 11; no improvement, 10. In other words, the failures did not exceed 20 per cent. Kennedy does not state the type of dysmenorrhoea in which oestrin was administered. Presumably the cases were unselected.

There is a type of dysmenorrhoea associated with fragments of menstrual decidua and an accentuation of the luteal phase which is fundamentally due to overactivity of the luteinizing hormone of the pituitary gland (Whitehouse's theory). Were it not for its removal from the circulation before the beginning of menstruation, the tranquilizing effect of the luteinizing hormone upon the uterine musculature would have rendered possible an easy separation of the menstrual decidua. There is abundant experimental evidence that oestrin overrides the action of the corpus luteum. Whether the effect is due to a direct inhibition of the corpus luteum hormone or to an indirect inhibition on account of the inhibiting influence of oestrin on pituitary function as a whole is an interesting theme for discussion. At any rate, according to Whitehouse himself, the beneficial action of oestrin in the type of dysmenorrhoea we are considering may be attributed to a deluteinizing effect upon the endometrial stroma. It seems to me that the results are too prompt to be due to an actual histological change in the stroma. A case which came under my personal care bears out this idea. The patient complained of pain which was premenstrual as well as intramenstrual. The menstrual blood contained fragments of menstrual decidua. Oestrin was administered in large doses several days before menstruation. The next menstruation was painless,

but definite fragments of the menstrual decidua could still be extracted from the menstrual blood.

In a previous communication[2] I referred to Reynolds's experiments upon female rabbits, which have definitely proven that under prolonged and excessive oestrin activity the myometrium becomes refractory to the normal adequate stimulus for that tissue. The results of these experiments provide an adequate explanation of the *modus operandi* of oestrin therapy. The failures in Kennedy's interesting series of cases are probably due to the fact that oestrin had not been administered in sufficient amount or over a sufficiently long period.

In the light of Reynolds's experimental results the administration of oestrin to cases of dysmenorrhoea due to a relative excess of oestrin circulating in the blood at the beginning of menstruation (Novak's theory) is not so paradoxical as it may seem.

A very satisfactory form of medical treatment is the administration of atropine sulphate in doses sufficient to cause mild saturation symptoms. Twenty years ago, Novak[10] was the first to advocate this form of treatment. An average dose of 1/120th of a grain of the sulphate, administered every four hours beginning from a day to several days before the period, in a large proportion of cases gives most gratifying results.

Should there be any evidence of constitutional disease, the latter should receive appropriate treatment. On account of the fact that the intensity of dysmenorrhoeic pain is accentuated by psychogenic factors, the physician should take time to reassure the patient as to the meaning and normality of the menstrual function. "I have always felt," says Novak, "that in many instances the mothers of dysmenorrhoeic young girls are in greater need of sex education than the patients themselves; for too often the girl at puberty is coddled into the belief that the menstrual period is a time of semi-invalidism and almost a species of segregation." Fairbairn, therefore, is in excellent company when he states that "he would put himself on the psychological side, especially in regard to treatment."

Surgical Treatment.

Dilatation of the cervix is the standard method of surgical treatment. Dilatation should be carried out to at least 11 Hegar. When the latter is passed, which is always difficult, dilatation up to 14 Hegar is a relatively easy procedure. A satisfactory explanation has not yet been given as to the ***rationale*** of this form of

treatment. "It would appear," says Eden, "that forcible dilatation exerts a powerful influence upon the mechanism of polarity by which the contractions of menstruation are so registered that they lose their tetanic or spasmodic character." Presumably, the natural dilatation of the cervix produced by labour exercises a similar influence upon the mechanism of polarity and is the explanation of the success of pregnancy in curing a certain proportion of dysmenorrhoeic cases.

In regard to the results of dilatation of the cervix, at the Edinburgh meeting it was reported that the number of permanent cures at the gynaecological centres varied from 50 to 60 per cent. I consider the percentage of permanent cures too high. At any rate, whether the results are permanent or temporary, there is general agreement that in many cases improvement does not follow dilatation. There are many cases, however, in which the patient is completely relieved of pain, and there is also a proportion of cases in which the patient is relieved, but not completely cured.

On the basis of the varying results of dilatation, I suggested in a previous communication[10] a division of cases into (1) those in which spasm of the circular muscle fibres surrounding the internal os is the characteristic feature; (2) those in which irregular contractions of the body of the uterus are the dominant feature; (3) and those in which irregular or tetanic contractions of the body of the uterus are accompanied by spasm of the cervical sphincter. In the first grouping we should expect complete relief after dilatation. In the second grouping we should expect little or no relief. In the third grouping we should expect relief, but not complete cure.

Resection of the presacral nerve is the most certain and permanent method of cure. This operation should be performed only for a severe type of dysmenorrhoea which has resisted all forms of treatment, including dilatation of the cervix. It is applicable to all types of dysmenorrhoea because most, if not all, painful impressions from the uterus travel via the superior hypogastric plexus. For that reason the success of the operation cannot be pressed into the service of any particular view in regard to the aetiology of dysmenorrhoea. It is the only rational treatment for dysmenorrhoea associated with disturbances of the bladder and rectum, because it relieves not only the dysmenorrhoea but also the cystalgia and rectalgia.

There seems a rather big discrepancy between the results of different operators. Davis[11] claims only 50 per cent of permanent cures. Cotte,[12] in a series of over 100 cases, claims 95 per cent

of permanent cures. I have myself resected the presacral nerve on 10 occasions without a single failure. Some of the recorded failures may be due to the fact that the operation has been performed for cases of pseudo-dysmenorrhoea. Most of the failures are probably due to faulty technique. Some operators remove the cellular matrix containing the nerve in the hope of not missing it. Not infrequently, however, the plexus may be divided into two parallel bands with an appreciable interval between them. Unless, therefore, we are enabled to appreciate the difference between the tough, unbreakable nerve fibres and the relatively fragile cellular tissue, we may easily miss one band of nervous tissue. It is true that at the promontory of the sacrum the plexus bifurcates into two well-defined nerves, the middle hypogastric nerves, which are unmistakable. It has, therefore, been argued that if the nerve is incompletely divided at the upper section, the division can be completed at the lower section. That is quite true, but we only succeed in resecting one band and merely dividing another which is sure to regenerate. Should failures occur in spite of correct surgical technique and the proper selection of cases (and I am not denying the possibility), then we can only surmise that in exceptional cases the afferent fibres of the *nervi erigentes* (parasympathetic) carry painful impressions, or, perhaps more painful impressions than normal, from the uterus as well as the appropriate impulses dealing with the emptying reflexes of the bladder and rectum. Unfortunately we cannot test the truth of this hypothesis as the parasympathetic supply to the bladder must be sufficiently intact to enable that organ to empty itself.

Should psychoneurotic symptoms be associated with dysmenorrhoea which is accompanied by vesical and rectal malfunction, in the interests of scientific truth and perhaps in that of the patient, psychotherapeutic treatment should be instituted; provided, of course, the pain can be relieved or rendered tolerable by medical treatment. Psychotherapy may not only relieve the patient of the mental symptoms, but it may permanently cure her physical discomforts.

Conclusions.

The special purpose of my paper is to remove the weeds which arrest the growth and development of the modern theories of dysmenorrhoea which I outlined in a previous communication. Some of these weeds are most difficult to eradicate; for they

have their roots deep down in the history of gynaecology. I refer in particular to Menge's version of the psychological theory of pain which he based upon a false philosophy and a false physiology.

I admit that a genuine psychological theory of dysmenorrhoea based upon Aristotle's theory of body-mind relation is a theoretical possibility. We shall have to depend, however, upon the results of psychotherapy in order to refute the hypothesis or convert it into an accepted theory. I also admit that psychological factors may augment the intensity of dysmenorrhoeic pain. Psychotherapy, therefore, may be a useful adjunct to the treatment of dysmenorrhoeic cases whether they rest upon a physiological or psychological basis.

Mechanical theories of dysmenorrhoea arise from a natural prejudice on the part of certain gynaecologists against psychological explanations; for between such explanations of functional dysmenorrhoea and mechanical explanations, there can be no *via media* from the point of view of psycho-physical parallelism.

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The Treatment of Functional Uterine Haemorrhage by means of Gonadotropic and Ovarian Hormones*

BY

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INTRODUCTION.

FOR the purpose of this paper the term "functional uterine haemorrhage" is used to denote a group of conditions characterized by uterine bleeding of variable type occurring in the absence of gross pelvic pathology. This type of bleeding is now regarded as a manifestation of a disorder of the endocrine system, and attempts have been made during the last six years to control or cure such haemorrhage by the rational use of hormonal preparations. Prior to this time several ovarian and placental products were used empirically for this purpose and good results were claimed. Thus Kohler[1] reported 74 per cent of successes with *agomensin*, and Keip,[2] Runge,[3] Reiprick,[4] Heynemann,[5] Sitz, Wintz and Fingerhut (quoted by Knab[6]), van Dougen[7] and others, obtained good results with *sistomensin* and *luteo-glandol*. However, it is now realized that these older preparations, of which those names are merely examples, contained little, if any, active hormone, and, moreover, the majority were administered orally, in the form of tablets—a procedure which could only seriously decrease any biological activity they may have possessed. Any good effects attending their use can hardly be ascribed to the relatively small quantities of oestrus-producing hormone which they contained. This communication is limited to a discussion of the value of potent, biologically standardized, and relatively pure preparations of the gonadotropic and ovarian hormones.†

* This communication includes a paper presented at the Tenth British Congress of Obstetrics and Gynaecology, April 2nd, 1936.

†Throughout this paper the following nomenclature will be used: *Oestrin, folliculin* or *follicular hormone*—to denote a group of oestrus-producing substances derived from follicular fluid, placenta, pregnancy blood or urine. At the same time it is realized that the use of these terms is traditional rather than scientifically exact. *Corpus luteum hormone*—progestin, corporein or secretory hormone. *Gonadotropic hormones, prolans A and B, prolan, anterior pituitary-like hormones*—to denote the ovary-stimulating hormones of the placenta, pregnancy blood and urine. The terms *anterior pituitary* or *hypophyseal hormones* will be reserved for those having their origin in the anterior lobe of the pituitary.

Extracts of other endocrine glands such as the posterior pituitary, thyroid, parathyroid, suprarenal, pancreas and pineal body, while appearing to be of value in the treatment of some cases of this disease, are not considered here.

The use of gonadotropic and corpus luteum hormones to control functional uterine haemorrhage developed as a result of the numerous discoveries of the last 10 years regarding the physiological and pathological relation between the pituitary, ovaries and uterus. The practical application of these advances was delayed for some time by the lack of pure potent preparations, but Martin[8] in 1930 was the first to report a series of patients treated with prolan; he was successful in 12 out of 13 cases. In the same year Siebke,[9] using praehormone B, recorded the successful treatment of one patient, and he later[10] claimed that he had commenced this type of therapy in 1927. Zondek,[11] also in 1930, stated that he had had good results with daily intravenous injections of 300 to 500 rat-units of prolan, but gave no detailed statistics. In the English-speaking countries the way was led by Novak and Hurd[12] who recorded excellent results following the use of the luteinizing hormone from pregnancy urine.

This form of treatment has had six years' trial, and in view of the divergence of opinion regarding its efficacy it would seem that the time is ripe for some assessment of its value. In this paper an attempt at such an assessment is prefaced by a brief description of the underlying endocrine disorders, and the immediate cause of uterine haemorrhage. The *rationale* of the treatment depends on these physiological and pathological considerations.

The Cause of Uterine Bleeding—Normal and Abnormal.

The cause of uterine bleeding has long been disputed, but although the problem is not completely solved, the essential facts are now accepted. As the results of experiments on immature, mature, and castrated monkeys carried out by Allen,[13] Maddux,[14] Morrell and others[15] Engle[16, 17, 18, 19, 20] Hisaw[21, 22] and Smith and Engle[23] the role of oestrin, corpus luteum and anterior pituitary hormones in the production of normal menstruation and pathological bleeding in these animals is known. Similar work was carried out on the human being by Kaufmann[24, 25, 26, 27, 28, 29] Loesser[30] and Clauberg[31] and it is now permissible to make the following statements without qualification.

1. A uterus, subjected to the action of oestrin, bleeds when

deprived of this hormone. The oestrin influence need not necessarily be removed completely but merely reduced.

2. Withdrawal from the uterus of a corporeal luteal hormonal influence has a similar effect.

3. Haemorrhage likewise results if the amount of a mixture of oestrin and progestin stimulating the uterus is diminished.

Two schools of thought have thus arisen on the problem of the cause of normal menstruation. The first believes that it comes about as the result of the premenstrual withdrawal, or diminution in amount, of the follicular and corpus luteum hormones in the circulation. The second postulates that the normal cyclical haemorrhage depends merely on the premenstrual fall in the blood-oestrin curve and bears no relation to the amount of progestin in circulation. The second view, frequently termed the Allen-Corner hypothesis, is fostered by several writers, amongst whom may be mentioned Moore,[32] Novak[33] and Allen[34]; the latter in 1935 reviewed[35] the evidence in its favour. Engle, Smith and Sheleanyak[20] also gave an excellent account of the facts supporting this theory, but conclude by stating their belief in the former of the two views. It certainly seems impossible to exclude the corpus luteum as a most important factor in normal menstruation, since it is proved that progestin can inhibit the occurrence of bleeding which usually follows a fall in the blood-oestrin level (Smith and Engle[23]). Recent investigations into this question include the demonstration by Okamoto[36] and Mayer, Merange and Israel[37] that menstruation can, to some extent, be delayed in its onset by the administration of oestrin to normal women, and the work of Hisaw[21] and Smith and Engle[23] who showed that the corpus luteum hormone can inhibit the onset of the menstrual flow in monkeys.

Whether the corpus luteum be involved or not, the cyclical rise and fall in the blood-content of ovarian pituitary hormones is almost certainly the result of an automatic and reversible interaction which exists between the pituitary and the ovary. This thermostat control, as Novak terms it, which has been postulated elsewhere[38, 39] and has recently been expounded by Moore,[32] may, on occasion, suffer interference by nervous stimuli which travel direct to the pituitary gland from the mid-brain.

Although a difference of opinion still exists about the importance of progestin as a factor in the production of normal menstruation there can now be no question that non-ovular bleeding—whether it be cyclical and closely approaching the normal in amount, or whether it be grossly pathological, is brought about

by a mere fall in the oestrin-content of the blood. The evidence for this is presented by Burch, Phelps and Wolfe[40] and by Tietze[41] in their complete descriptions of endometrial hyperplasia, and is so strong that the view is no longer disputed. Hisaw[21] in his experiments on monkeys noted that the amount of uterine haemorrhage is to some extent directly proportional to the quantity of oestrin previously administered.

CLASSIFICATION OF FUNCTIONAL UTERINE HAEMORRHAGE.

Numerous attempts have been made to classify functional uterine haemorrhage into various sub-groups, but all are unsatisfactory for one reason or another.

(*a*) *Classification depending on Age Incidence.*

This is frequently used, and puberty, adolescent, premenopausal, menopausal and postmenopausal haemorrhage, are well recognized clinical terms. Novak[42] says that more than 50 per cent of cases of functional uterine haemorrhage occur at the menopause, 5 to 10 per cent at puberty, and 35 per cent between the ages of 20 and 40.

(*b*) *Classification depending on Clinical and Pathological Features.*

(i) *Metropathia haemorrhagica.* This is a disease seen most frequently at the extremes of active sexual life, and its typical symptom is metrostaxis, with or without a preceding period of amenorrhoea. The endometrium shows hyperplasia—that is, an exaggeration of the interval phase—and there are one or more follicular ovarian cysts. The endometrial changes are brought about by a prolonged or excessive stimulation by oestrin, and an absence of corpus luteum influence; the evidence in favour of this contention needs no repetition since it is reviewed in the monographs of Burch, Williams and Cunningham,[43] Tietze[41] Zuckerman and Morse,[44] and others. It was confirmed more recently by the production of endometrial hyperplasia in human castrates which was carried out by Kaufmann,[25] Werner and Collier,[45] Szarka,[46] and Damm.[47] Kaufmann states that five times as much hormone is required to produce hyperplasia as to bring about the normal endometrial proliferation of the interval phase.

However, it may be *continued* administration of oestrin rather than the injection of large amounts which brings about hyperplasia (Werner and Collier,[45] Simpson and Burch[48]). Hisaw[21] even suggests that it is caused by an unusually *small* amount of oestrin which is acting for an abnormally long period of time, and that it is the low level of the blood-oestrin which prevents

liberation of the hypophyseal luteinizing hormone and consequent corpus luteum formation. Whether or no this be true, if the amount of oestrin acting on the uterus is increased, or remains constant, amenorrhoea persists, and bleeding only takes place when the oestrin level in the blood falls. This accounts for the amenorrhoea preceding the haemorrhage in metropathia haemorrhagica.

It should also be mentioned that since normal ovulation is dependent on the anterior pituitary gland, it is almost certain that follicular ovarian cysts, with the consequent disturbance in oestrin production, endometrial hyperplasia and non-ovular uterine haemorrhage, are brought about by a primary pituitary disorder (Hofbaeur,[49] Engle,[17, 20] Smith and Rock,[50] Smith,[35] Fluhmann[51] Novak and Hurd,[12] Potter,[52] and others).

(ii) *Epimenorrhoea and epimenorrhagia, or polymenorrhoea.* The names indicate the type of bleeding, and it is associated with a rapid ovarian cycle and frequently with the simultaneous ripening of more than one Graffian follicle. In contradistinction to hyperplasia, the endometrium in these cases goes through the normal cyclical phases, but each phase is shortened in duration.

The cause of the excessive bleeding is unknown, but it is assumed by most workers that the corpus luteum is underactive. There is very little evidence in favour of this view since in my instances more than one active corpus luteum is present at the same time, and it may well be that the heavy loss in epimenorrhagia is due to the sudden withdrawal of an unusually strong lutein influence. Be this as it may, all are agreed that the shortening of the cycle is essentially due to premature degeneration of the yellow body.

This disease is also primarily of pituitary origin, and this accounts for the fact that its onset frequently dates from pregnancy, that is, from a time when pituitary function is profoundly disturbed.

(iii) *Menorrhagia, or hypermenorrhoea.* This condition represents, in many cases, a form of non-ovular bleeding; in others, its mechanism is, so far, unknown.

This classification does not include some of the rarer types of haemorrhage, such as excessive bleeding occurring at infrequent intervals, due to a prolongation of either the luteal or oestrous phases, ovulation bleeding, and other forms of intermenstrual loss which are brought about by temporary diminution in oestrin production.

(*c*) *Pathological Classification.*

A third possible classification is one based on pure pathology and involves a division of functional uterine haemorrhage into at least three groups. This is theoretically the most satisfactory classification, but it has obvious clinical limitations.

(i) *Bleeding from endometrium in the interval phase,* often in the state of hyperplasia. This includes metropathia haemorrhagica, non-ovular bleeding, most cases of metrostaxis and some of menorrhagia or excessive bleeding at frequent intervals. This type of bleeding occurs most frequently in adolescence or in patients approaching the menopause.

(ii) *Bleeding from premenstrual endometrium.* In this group are included patients suffering from epimenorrhoea and epimenorrhagia, and some cases of menorrhagia and excessive bleeding at frequent intervals.

(iii) *Bleeding from an endometrium showing mixed phases.* This is seen in conditions known as irregular ripening and irregular shedding of the endometrium. Irregular ripening is believed to be due to a persistently low level of oestrin, while irregular shedding may be due to a deficiency of the corpus luteum. Traut and Kuder[53] are responsible for the recent interest taken in these conditions, but their estimate that they constitute 20 to 30 per cent of all cases of functional haemorrhage is probably much too high. The conditions exist, but are rare, and a few cases of menorrhagia and irregular continuous bleeding belong to this group.

These classifications, in particular the second one, assume that the type of haemorrhage is some indication of the exact underlying pathology. This assumption is questioned by Anspach and Hoffman[54] and by Sevringhaus and colleagues,[55] but the findings of workers who investigated large series of cases (Shaw,[56] Cannon,[57] Potter,[52] Fluhmann and Morse[58]) definitely support it. Goecke[59] also recently published statistics in favour of this view, and showed that in a series of 146 cases of endometrial hyperplasia the symptoms were as follows: continuous haemorrhage 127, intermenstrual haemorrhage 10, menorrhagia 8, and preliminary amenorrhoea in the majority. Siebke,[10] Runge[60] also think that endometrial hyperplasia gives rise to continuous, rather than cyclical bleeding. Even Anspach and Hoffmann,[54] who deny any relation between pathology and symptomatology, found endometrial secretory activity in six out of seven patients suffering from cyclical bleeding, whereas it was present in only 33 per cent of all cases of functional haemorrhage. Of

the 80 patients whose treatment is described here, the endometrium was examined in 29, and the following conclusions were drawn:

	Non-ovular bleeding	Ovular bleeding
Metrostaxis	21	2
Epimenorrhoea or epimenorrhagia ...	1	3
Menorrhagia	1	1

There appears, therefore, no reason to believe that a study of the symptoms is not a good guide to the underlying endocrine upset in any particular patient.

Unfortunately, since hyperplasia of the endometrium is the most clearly defined clinical and pathological entity in this group of disease, there is at present a tendency to consider that the majority of haemorrhages, if not all, are due to this condition, and are caused by an excess of oestrin and a deficiency, if not a complete absence, of the corpus luteum hormone. In particular, those writers dealing with organotherapy adopt this attitude. Novak[42] in most of his writings says that endometrial hyperplasia associated with follicular ovarian cysts is present in nearly all cases, and even states[33] that the finding of a secretory endometrium means that the case is not one of functional uterine haemorrhage. King[61] affirms that hyperplasia is present in 80 per cent of all cases, and Keene[62] says that in the majority excessive and prolonged follicular stimulation is the characteristic feature, although he emphasizes that all cases are not identical. Yet no evidence is brought forward to support these views, whereas all the published pathological investigations prove that only one half or less of all cases of functional uterine haemorrhage are due to endometrial hyperplasia (Shaw,[56] Potter,[52] Anspach and Hoffmann,[54] Plass[63]). Fluhmann[64] found hyperplasia in 66 per cent, but the evidence, for the most part, supports the view of Henderson[65] who says that hyperplasia is present in not more than one third of the patients.

This tendency to regard all excessive bleeding at all ages as being due to hyperplasia is a real danger and is already exerting an adverse influence on attempts at organotherapy. The warning lately issued by Traut and Kuder[53] that the diagnosis of endometrial hyperplasia is becoming as popular and as misleading as the diagnosis of endometritis in the last century, is a timely one.

Nevertheless, there is general agreement that a large percentage of pubescent and adolescent cases are due to hyperplasia, as are many examples of menopausal haemorrhage. Kaufmann[25, 29, 66]

says it is present in practically all bleedings at these ages, and Heynemann[5] found it present in 80 per cent of 31 cases of juvenile bleeding. Potter's[52] findings confirm this, and Kane[67] and most authorities imply that pubescent haemorrhages are, for the most part, non-ovular in type.

It would appear, therefore, that 80 per cent of pubescent haemorrhages are non-ovular and are usually associated with endometrial hyperplasia, a large proportion of the menopausal haemorrhages also conform to this type, but the bleeding at intermediate ages may be of any kind, so that of the total cases not more than 50 per cent exhibit non-ovular bleeding.

Rationale of Treatment.

Since hyperplasia and the accompanying haemorrhage are brought about by an unopposed action of oestrin, its treatment necessitates either the administration of the missing corpus luteum hormone or the production of an active corpus luteum in the patient's own ovary. The former treatment is obviously replacement therapy, and while it should be successful its good effect should only persist for the period of its administration. The second type of treatment theoretically has the advantage since it may re-establish the normal function of the ovary. In the early days of this work a luteinizing hormone prepared from pregnancy urine or placenta was used for the most part, and proprietary extracts of pregnancy urine are still favoured by the majority of clinicians. In some cases the blood or urine from pregnant women are used as therapeutic agents; these are less expensive than proprietary preparations and are believed to depend for their action upon their prolan content.

Within the last few years corpus luteum has become available for clinical use, and reports of its value in the treatment of functional uterine haemorrhage are already at hand. A still more recent modification is the simultaneous administration of corpus luteum and gonadotropic hormones, thus combining replacement and stimulation therapy

Again, if the haemorrhage is arising from an endometrium in the pregravid state, as in epimenorrhoea, and is due to premature degeneration or underactivity of the corpus luteum, premenstrual stimulation of the ovaries with luteinizing hormone, or premenstrual replacement therapy with progestin, is treatment having a sound basis. This principle was recently expounded by Meigs[68] and Runge,[60] and additional evidence supporting the use of corpus luteum preparations in these cases lies in the demonstration by

Hisaw[21] and Smith and Engle[23] that normal menstruation can be delayed in monkeys by the administration of corporein.

If follicular cysts, and the consequent endometrial hyperplasia and non-ovular bleeding, are primarily due to a pituitary disorder, it may seem irrational to administer gonadotropic hormones in their treatment. However, most preparations of these hormones contain essentially the luteinizing fraction, and although they are loosely termed "anterior pituitary hormones" they in no way deserve this designation since they are not obtained from this gland, and their active principles, although they resemble the pituitary hormones in some of their actions, are not identical with them nor are they produced by the same endocrinous organ. These differences have been recently proved and emphasized by Smith,[35] and Hamburger,[69] Hinsey and Markee,[70] Fluhmann,[71] Richert and others,[72] Hill and Parkes,[73] Evans and others,[74, 75] Selye and others.[76] Zondek[77] now believes that these hormones are not identical, and Engle,[16, 17, 18, 19, 20] in reviewing all the evidence, says that the existence of a difference is now beyond dispute.

Functional uterine haemorrhage has also been treated by the administration of oestrin for the following reasons:

1. It is the only hormone available to some workers. This was true prior to the last few years, and Fluhmann[64] in 1929, and Goldtsine and Fogelson[78] admitted that they used oestrin simply because corpus luteum was not available. This reason is no longer valid in this country.

2. To improve the tone of uterine muscle and hence control menorrhagia. Runge[3, 79] and Siebke[80] administer the hormone with this object.

3. To restore the vitality of the endometrium in cases of functional uterine haemorrhage associated with endometrial atrophy (Martius[81]).

4. To depress follicular activity in the ovary. There is no doubt that experimentally it is possible to show that oestrin has this effect and it is probably brought about via the pituitary—as postulated by Moore[82] and Nelson.[82] Clauberg and Breipohl,[83] Westman,[84] Burger[P.5] also believe that the follicular apparatus of the ovary may be inhibited by oestrin, and Dahlberg[85] recently reviewed the evidence in favour of this view.

5. Oestrin may not only inhibit follicular activity but may bring about corpus luteum formation by setting free the luteinizing hormone from the hypophysis. Clauberg,[86] Knab,[6] Witschi and Levine,[87] Kurzrok, Wilson and Cassidy[88] state this possibility, and

Westman,[84] Wolfe,[89] Baumann[90] and Hisaw and others[91] claim to have demonstrated this occurrence in animals.

However, if non-ovular bleeding is always due to a decrease in the level of blood oestrin, administration of this hormone should raise that level and, theoretically, should result in temporary control, followed by exacerbation of the haemorrhage when treatment is suspended. This hormone is, therefore, indicated to prevent the occurrence of so-called "ovulation haemorrhage" which is always due to a temporary and slight fall in the oestrin-content of the blood but, until the more intricate theories outlined above are more definitely established, the administration of oestrin to control the more usual forms of haemorrhage is theoretically unsound. Exception to this rule may be made if the endometrium is atrophic, but such a finding is rare and its occurrence is not yet understood.

Again there is no scientific basis for the treatment of haemorrhage from a premenstrual endometrium by means of oestrin, since it has been shown both in monkeys (Smith and Engle[23]) and in the human subject (Kaufmann[66]) that oestrin, even if given in the largest doses, cannot prevent the onset of bleeding which follows corpus luteum withdrawal.

Results of Treatment.

In an attempt to assess the value of endocrine treatment, results and opinions have been obtained from three sources:—

1. *Results Collected from Literature.* (Tables I, II and III).

The collection of published results is associated with many difficulties. The number of communications dealing with organotherapy is immense, but the number of recorded cases is comparatively small. Many authors mention that they have treated several hundreds of patients successfully, but they make no attempt to give details, and others base their conclusions on isolated cases. Extravagant claims, unaccompanied by clinical notes, are common, and create the impression that they are handed on as unverified statements from one writer to another. After a close search, and excluding articles in which not more than two cases are described, records (and some of these are very incomplete) of only 594 cases have been traced. Comparison of individual statistics is not always easy, since different commercial preparations are used by different observers; some series of cases are grouped on a pathological, others on a clinical, basis, while many are presented without any attempt at classification. Moreover, the after-histories of the cases described are frequently omitted.

In view of these difficulties the author has been forced to

abandon all attemtps to subdivide reported cases on any basis whatsoever, but in Tables I, II and III an endeavour is made to include any important comments of the quoted authorities.

In addition to those mentioned in these Tables most writers ([92—99, 4, 81], and others) emphasize the value of treatment with gonadotropic hormones, and only a few, such as Geist and Spielman,[100, 101] Shaw[102] and King,[61] doubt their efficacy.

The use of standardized corpus luteum hormone is confined to very recent years and all results so far published in the continental literature. Besides those mentioned in Table II, several authors, Kaufmann,[25] Richelt,[103, 104] Guggisberg,[105] Gerhardt,[106] Runge,[107] Kaute,[108] Marselek,[99] Clauberg,[109] report that progestin therapy is attended with happy results.

In Tables I, II and III the failures are all recorded as such in the original articles; the cures include not only patients whose menstrual irregularity was permanently corrected, but also several in whom the bleeding was adequately controlled initially but in whom it recurred subsequently: these latter are also entered as "relapses". Those cases indicated as "improved" exhibited either partial relief from symptoms or were completely relieved for a very short time. Some patients in this group are similarly described in the original articles, but others, as a result of the study of the reported case histories, are denoted as "improved" for the purpose of this paper only.

2. *Liverpool Results.*

In Tables IV, V and VI are presented the results of the treatment of 79 patients by means of the gonadotropic hormones of pregnancy urine. These patients were treated between 1932 and 1935 by individual workers (A. L. Robinson, J. St. G. Wilson, Ruth Nicholson, J. W. Burns, A. A. Gemmell, M. Datnow, S. B. Herd, and the author) in Liverpool, and I wish to thank my colleagues for their permission to record these cases and for all the assistance which they have afforded me in investigating the after-histories. Table VII indicates the periods of time for which patients were observed. Nine patients in whom organotherapy failed had operative treatment, and their subsequent history is irrelevant. Of the remaining 70 patients, 59 were traced after periods of three or more months, and 25 after the elapse of one or more years, after treatment.

The results are arranged in three groups according to the ages of the patients; a purely pathological classification, although preferable, is impossible, since a study of the endometrium was

carried out in only a small proportion of cases (28 out of 79). In addition to the results tabulated, one further patient was treated with proluton. Her age was 23 years, and she had had metrostaxis for 14 days. Four daily injections, of two clinical units each, brought about complete cessation of bleeding, and menstruation has been regular for the ensuing four months. The bleeding in this case was proved by diagnostic curettage to be non-ovular.

Technique.

With the exception of one case in which pregnyl was used in addition, all patients received gonadotropic hormones in the form of antuitrin S. This was given, for the most part, in daily intramuscular injections of 1.0 c.c. (100 rat-units) until bleeding ceased. For cyclical haemorrhage the same dose was administered daily for three or four days prior to the expected onset of menstruation, continued throughout the duration of the menstrual loss, and repeated for two or three periods. This technique is recommended, with slight modifications, by most writers (Meigs,[68] Novak and Hurd,[12, 35] Smith and Rock,[50] and others) and there is a general insistence that the treatment is best given while the bleeding is in progress. In some cases, however, patients received injections at irregular intervals, or at intervals of two to seven days: this faulty technique explains some of the failures. Other patients received injections of 0.5 c.c. or 2.0 c.c., but none were given more than 3.0 c.c. in a single dose. The details of dosage are shown in Table VIII.

Four patients had curettage performed for the bleeding, and the treatment with antuitrin S was given daily after the operation as supplementary therapy. Campbell[110] recommends curettage as an adjunct to hormone treatment, and Siebke[10] records 42 cases (not included in Table I) of pubescent bleeding treated prophylactically with gonadotropic hormones, after curettage. He claims good results since only six patients had a recurrence of symptoms. Runge[60] also prefers to use gonadotropic hormones together with curettage. However, no matter how successful the practice of therapeutic curettage may be, it certainly interferes with attempts to estimate the value of organotherapy, and the results in the four patients mentioned, although good, are recorded in Tables IV, V and VI as being doubtful.

3. *Replies to a Questionnaire.*

In response to a questionnaire 44 replies were received from

foreign clinics; the opinions submitted are collected in Tables IX and X. The author wishes to express his gratitude for the help received from these foreign authorities, mentioned by name under "personal communications," and to thank them for the care and thought expended on their replies. Nine of those who replied do not use organotherapy, or only employ endocrine substances (such as thyroid) which are not relevant to this paper. A tenth foreign observer (English[P.14]) uses these hormones on such few occasions and obtains such inconsistent results that he prefers not to express an opinion on their merits.

Only views expressed in the remaining 34 replies are considered here. Nevertheless, the fact that this method of treatment is still not accepted by so large a proportion of clinics, is of some significance, especially in view of the conclusions ultimately reached as a result of this inquiry.

Discussion of Results.

Gonadotropic Hormones.

(*a*). *Control of Bleeding.*

Consideration of Table I reveals extraordinary variations in results. The percentage of cures varies from 100 to 28, and is 69 for the whole series. Some writers are much impressed with this method of treatment while others consider it almost useless. There is a suggestion in recent reports (Ehrhardt,[111] Novak[35]) that others have noticed this lack of uniformity in results.

In this connexion, inquiry into the details of recorded cases shows that individual criteria of success vary, and many patients described by a particular writer as being cured would be viewed by another observer as showing no response to treatment. Moreover, the estimation of results is always clouded by the fact that functional uterine haemorrhage is a condition which is likely to cease spontaneously, and it is impossible to control results except by amassing large numbers of cases.

Other factors contributing to the variation in results are the differences in the individual techniques and dosage and the inconstant potency of the preparations used, as emphasized by Novak and Hurd.[12] Nevertheless, it is likely that the total figures of reported results, as presented here, give a more accurate conception of the value of the treatment than do the claims of individual writers each basing his conclusions on small numbers of cases.

It is of interest to note that the number of successes obtained

(63 per cent) in Liverpool closely approximates to the average cure rate of the total number of cases (69 per cent). Three of the 15 failures and one of the 14 doubtful results were probably due to faulty technique in the conduct of the treatment, and in another patient in which treatment failed pelvic adhesions were found at subsequent laparotomy.

The opinions expressed in reply to the questionnaire (Tables IX and X) are illuminating and provide the final and conclusive proof that this form of treatment does not satisfy the claims which, hitherto, have been made for it. Of 27 authorities using gonadotropic hormones, only five report consistently good results (in specially chosen patients), 14 note poor or fair response, and two of these, Maguire[P.25], Plass[P.34], prefer to use thyroid extract. Eight emphasize the variation in results, and one, Stander[P.37], believes that all the so-called cures are merely spontaneous, and in no way connected with the treatment. From these figures the only possible conclusion is that clinicians in general are coming to regard even this type of organotherapy as being unreliable, and although it may produce some brilliant results, it is by no means rare to see patients who show no response to it.

(*b*). *The Time and Dosage Required to Control the Bleeding.*

It is frequently stated that three or four days' treatment is all that is required if the case is one of metrostaxis, but Campbell[110] points out that the bleeding may not be controlled until one or more weeks have elapsed, and Gabrielianz[112] says that treatment for five months may be necessary. Runge[3] reports two cases; the first was cured by one injection of prolan in one day, but the second did not respond until treatment had been continued for a week. It seems that the time factor varies from case to case rather than from author to author, and Meigs[68] states definitely that it may take one to 20 days to bring about a cure. However, when so long a time is required, there arises a serious doubt as to whether the treatment and the cure have any direct connexion or whether they are merely incidental, and in the Liverpool series cessation of bleeding more than three weeks after commencement of treatment is classified as a doubtful result. Out of 30 cases of metrostaxis cured by treatment, bleeding ceased in 24 after one to six daily injections, and the remaining six patients responded after 10 to 21 daily administrations.

In cyclical haemorrhage a cure is usually apparent within

the space of three to four menstrual periods, although Meigs[68] says that treatment for six to eight months may be required.

Foreign clinics also experience variations in the time of response to treatment, and whereas six say that a cure is quickly obtained, an equal number comment on the inconsistencies and variations in response.

(*c*). *Type of Haemorrhage showing Best Response.*

Some difference of opinion is again noted regarding the relative value of gonadotropic hormone therapy in the relief of different forms of haemorrhage. Thus Gabrielianz[112] obtained the best results in epimenorrhagia (only four cases), Henderson[65] in menorrhagia, and Goezy[113] in cases of cyclical, rather than acyclical, bleeding. However, apart from these, the majority of observers find that metrostaxis with or without a preliminary period of amenorrhoea, as experienced in metropathia haemorrhagica, endometrial hyperplasia and non-ovular bleeding, shows the best response (Neumann,[114] Meigs,[68] Runge,[60] Novak and Hurd,[12] Witherspoon[115]). Anspach and Hoffmann[54] also obtained good results in cases of irregular haemorrhage, and Siebke[10] confirmed the presence of hyperplasia in all his cases prior to treatment. Tables IV, V and VI, giving details of Liverpool cases, show conclusively that the results in metrostaxis, irrespective of the age of the patient, surpass those obtained in other forms of haemorrhage. However, among the patients aged 20 to 40 (Table V) it will be seen that six of the failures were proved to have had non-ovular haemorrhage. Nevertheless, in each of these cases some other factor such as faulty technique, large endometrial polypi, etc., accounted for the lack of success attending the treatment. The especial value of gonadotropic hormones in cases of this type is confirmed by the opinions expressed in reply to the questionnaire. Only three authorities believe that all types of haemorrhage benefit, but 10 state that metrostaxis, hyperplasia, or non-ovular bleeding, show by far the best response.

(*d*). *Relation of Results to the Age of the Patients.*

With regard to this question, agreement is more general. Anspach and Hoffman,[54] Westman,[84] Goezy,[113] Johnstone, Wiesner and Marshall,[96] Martius,[81] Ehrhardt,[111] Siebke,[10] all state that the best results are obtained in patients under the age of 20, and Lawrence[116] obtained 100 per cent success in 10 cases of pubescent haemorrhage. This latter figure needs qualification, however, since menstruation did not return to normal in some

of the patients until treatment had been continued, on and off, for two years. Siebke's excellent results[10] were obtained in patients of adolescent age.

Fifteen out of 25 foreign authorities (Tables IX and X) note that patients of pubescent or adolescent age give by far the best results, and several others imply this opinion without making a definite statement. However, Neumann[114] thinks that the cures of pubescent cases are all spontaneous and have no connexion with the treatment, and he infers that the best results are seen in later life.

As regards the cases recorded in this paper, treatment was successful in 77.7 per cent at puberty, but only in 61.2 per cent and 50 per cent at later ages. This age preference is probably accounted for by the fact that practically all the pubescent cases are examples of non-ovular bleeding with endometrial hyperplasia, whereas other types of functional uterine haemorrhage are relatively more common in later life. It is somewhat strange, however, that menopausal haemorrhage, which again is usually non-ovular, shows an inferior and variable response. This failure to react to treatment of patients approaching the climacteric, is mentioned by Meigs,[68] Kane,[67] Rongy, Tamis and Gordon,[117] Westman,[84] and is emphasized by the results shown in Table VI and the views tabulated in Table IX. The reason for it is unknown, but is mentioned again later.

(*e*). *Amenorrhoea as the Result of Treatment.*

An interesting feature of the cured cases is the occurrence of amenorrhoea, usually lasting for one to six months, following cessation of bleeding. This is noted particularly in pubescent cases and is recorded by Campbell,[110, 118] Novak and Hurd,[13] Westman,[84] Witherspoon,[115] Smith and Rock,[50] Geist and Spielman,[101] Scott and Watson[P.36], McLeod[P.30], MacKay[P.29] and Westman[P.44]. Campbell[110] also observed it in some menopausal cases. It was formerly thought that this symptom indicated excessive luteinization of the ovaries; this is now known to be untrue and its occurrence does not depend on the amount of hormone injected. Non-ovular bleeding normally alternates with periods of amenorrhoea, and there is no evidence to disprove the probability that the amenorrhoea is an accident bearing no relation to the treatment, but representing the usual sequence of events in non-ovular haemorrhage at puberty and the menopause. Smith and Rock[50] state that "amenorrhoea and delayed menses occurred often enough in relation to treatment to seem to be

caused by it," the more general opinion is that of Geist and Spielman,[101] who regard it as being incidental.

In the Liverpool series (excluding those patients who became pregnant) amenorrhoea of three to six months in duration was noted following treatment in nine patients: of these five were under 20 years of age.

(*f*). *Increased Haemorrhage as the Result of Treatment.*

Several writers, Smith and Rock,[50] Burch and Burch,[119] Henderson,[65] Runge,[3, 60] note that one of the responses to treatment is a temporary increase in flow which takes place after the first one or two injections, and that this usually indicates the impending cessation of bleeding. Ehrhardt[111] records exacerbation of haemorrhage during the treatment of a patient at puberty and the use of gonadotropic hormone was substituted by that of oestrin before it was controlled. This increased haemorrhage was not seen in any of our cases recorded as failures, but it was not infrequently present after the second or third injection in patients who were subsequently cured. The reason for this is discussed later.

(*g*). *Effects of Treatment on subsequent Menstrual Function: Are the Results Permanent or Temporary?*

A cure is usually followed by return to the normal menstrual rhythm with or without an intervening period of amenorrhoea. However, there is no doubt that a recurrence of symptoms is common; such relapses are often seen in menopausal, and not infrequently in pubescent cases, and are recorded by most observers—in particular, Campbell,[110] Meigs,[68] Westman,[84] Anspach and Hoffman,[54] Novak and Hurd,[12] Henderson,[65] Neumann,[114] Elden,[120] Geist and Spielmann,[100, 101] Smith and Rock.[50] Lawrence[116] observed several relapses and many of his pubescent cases required treatment, on and off, for two years. Of the 50 cured patients in the Liverpool series 14 had a recurrence of bleeding (within six months in eight patients and within one year in 13).

Although it is frequently stated that the advantage which the use of gonadotropic hormones has over other methods of treatment such as curettage or even the administration of corpus luteum (Westman,[84] Martius[81]), is that the disordered ovarian cycle is permanently corrected, the statistics presented in the accompanying tables provide no confirmation of this. On the contary, the high proportion of cases which relapse is a clear indication that

the success of treatment is purely temporary. Novak, who in 1931[12] professed himself unable to say whether the results were permanent, now asserts[42] that the effect applies only to the particular attack of haemorrhage for which organotherapy is instituted. Neumann[114] and Meigs[68] also conform to this opinion. The replies to the questionnaire (Tables IX and X) provide further confirmation of this view; there are no observers who say that gonadotropic hormonal therapy is consistently permanent in its effects, two say it is probably permanent, and a third that it produces permanent cures in pubescent cases only; the remaining 21 replies (88 per cent) indicate that it is purely temporary in action or very variable in its remote effects. It would seem that the subsequent menstrual history of most patients resembles that of those who receive no hormonal treatment for this disorder. All these cases of functional uterine haemorrhage are temporary with a tendency to spontaneous recovery, but there is, in all, a distinct possibility of a recurrence of haemorrhage or periods of amenorrhoea. It may be that the more frequent and more rapid occurrence of relapses in menopausal patients explains why this form of treatment is apparently of less value in their cases than it is in the control of anovular haemorrhage in early life.

There is, therefore, no evidence to show that gonadotropic hormonal therapy can have any effect on menstrual function other than to control the particular attack of haemorrhage for which it is applied. Nevertheless, such treatment always preserves, or at least does not affect adversely, the menstrual function, and for that reason is preferable to more radical procedures.

(*h*). *Effect of Treatment on Reproductive Function.*

Four of the patients whose treatment is reported here became pregnant within a few weeks or months of the control of haemorrhage. This is not evidence that such treatment improves the chances of conception, but it implies that the ability to conceive, which is ordinarily decreased in patients suffering from functional uterine haemorrhage, is not adversely affected. Of 27 authorities replying to the questionnaire, all agree that pregnancy is unaffected, four believe that the chances of conception are probably increased, but the remainder either offer no comment on this point or state definitely that there is no evidence that conception is influenced in any way by gonadotropic hormonal therapy.

Corpus Luteum Hormone.

(*a*). *Control of Bleeding.*

The small number of cases so far recorded makes it difficult to draw definite conclusions but indicates that individual results vary (Table II) and that only 68 per cent are cured by administration of corpus luteum. It is significant that the percentage cure-rate is exactly the same as that for treatment with gonadotropic hormones. Opinions as to the merits of corpus luteum hormonal therapy vary considerably, and whereas Kaufmann[25] says that by its use even the most severe forms of haemorrhage may be controlled, Damm[121] emphasizes that results are variable, some excellent and some disappointing. Westman[84] records success with prolan in a case in which lutex had originally failed to control the bleeding, and Damm,[121] using pregnancy serum, notes the cure of a patient who had not responded to a corpus luteum preparation.

The same difficulty* is encountered in assessing the results of corpus luteum therapy as is mentioned in the discussion of the use of gonadotropic hormones, but the similarity in recorded statistics and case histories indicates that equally good responses are obtained with corpus luteum, as with gonadotropic, hormones, and although one may succeed where the other fails, the positions may equally well be reversed.

This opinion is supported by the comments of observers which are set out in Tables IX and X. Of 15 clinics employing this treatment, only five report good results, and three of these use it in specially chosen cases. Two say the effects are variable,

* Additional complications arise owing to the use of different units in the descriptions of dosage. This discord is unusually obvious in connexion with the corpus luteum hormone. The potency of preparations of this principle is expressed in rabbit-units, but two different rabbit-units are recognized—the Clauberg and the Allen-Corner unit respectively. Moreover, the relation of one to the other appears to be unknown. Thus Kurzrok, Wilson and Cassidy[88] say that the A.C. rabbit-unit is four times as large as the C. rabbit-unit, whereas continental workers claim that the latter is more potent. Messrs. Schering Ltd. (quoted by Biskind[35]) actually assert that the C. rabbit-unit is three times as powerful as the A.C. rabbit-unit, while Corner[35] is of the opinion that it has only half the activity. To make matters more difficult some commercial preparations are standardized in clinical units—each one representing a fraction of a rabbit-unit.

At a League of Nations Conference in 1935 an "International Unit"—defined as being equal to the activity of one milligram of B-progesterone—was introduced. This unit is approximately equal to the A.C. rabbit-unit.[35] So far, however, it has not been generally adopted.

another that cures are spontaneous rather than related to therapy, and the remaining eight state that the responses observed are poor. In view of this there seems very little reason for any assertion—such as is frequently made—that corpus luteum produces brilliant and consistent results in all cases.

(*b*). *The Time and Dosage required to Control Bleeding.*
(*c*). *Type of Haemorrhage showing Best Response.*
(*d*). *Relation of Results to Age of Patient.*
(*e*). *Amenorrhoea as the Result of Treatment.*

The effects of corpus luteum resemble very closely those of the gonadotropic hormones in respect of these four headings. The duration and amount of treatment which is necessary is inconstant, and cannot be foretold. Runge,[107] Scheidt,[122] Martius[81] all state that one to three C. rabbit units daily for one to fourteen days are sufficient in most cases, but enormous doses are frequently advised for difficult cases. Thus Kaufmann[25] records a patient who received 450 C. rabbit units within two months before bleeding was controlled. Messrs. Schering Ltd. recommended 20 clinical units of proluton daily if the haemorrhage continues in spite of previous daily administrations of two clinical units.

Treatment is of more value in metropathia haemorrhagica and non-ovular bleeding than in other forms of haemorrhage. This is stated by Marsalek,[98] Scheidt'[122] and implied by most writers. It is confirmed by opinions from foreign clinics, for of these five limit the employment of corpus luteum therapy to cases of this kind, and only two think it equally advantageous in all forms of functional uterine haemorrhage. However, Runge[60] uses it more especially for epimenorrhoea and prefers gonadotropic hormonal therapy in non-ovular bleeding.

Pubescent cases show the best response (Clauberg,[109] Knab[6]) and although Westman[84] recommends the use of lutex at the menopause he was successful in only four out of nine patients. However, Kaute[108] notes that heavier dosage is required for patients of adolescent age. Tables IX and X indicate that four clinics consider that pubescent haemorrhage is the best indication for its administration, eight infer that all cases benefit, and one reserves its use for patients in the era of sexual activity.

Amenorrhoea occasionally follows cessation of bleeding (Damm,[121] Westman[84]): there is no evidence to show that this occurrence bears any relation to the treatment, and for reasons

stated in the discussion of gonadotropic hormonal therapy it is almost certainly spontaneous.

(*f*). *Is the Cure Temporary or Permanent?*

Since this type of treatment is purely replacement of the lacking hormone, any response other than a temporary one is not to be expected, and Kaute,[108] Westman,[84] Marsalek[98] emphasize that the results obtained support this view. The last writer records that 22 per cent of cases have a recurrence of symptoms. Of those authorities replying to this question, six say the effects are temporary, two think they *may* be permanent, and two point out that there is great variation in remote results of treatment. There seems no doubt, therefore, that corpus luteum therapy is purely temporary in its actions, and in this respect suffers from the same disadvantage as does gonadotropic hormonal treatment.

(*g*). *Effect of Treatment on Reproductive Function.*

So far as can be ascertained at present, this form of organotherapy has no effect of any kind on subsequent conception, pregnancy, or parturition. Replies to the questionnaire indicate that only four foreign observers believe in the possibility of the treatment improving the chances of conception; all others are agreed that conception and pregnancy are uninfluenced, or state that there is no evidence on which to base an opinion.

Oestrin.

In 1931 Zondek[11] claimed that the most severe haemorrhage can be controlled by intravenous medication with oestrin. Spiegler[123] and Siegert[124] report good results following the use of comparatively small doses of oestrin in cases of excessive uterine haemorrhage: nevertheless their patients probably had chronic inflammatory lesions in the pelvis and were not examples of true functional bleeding. Runge[60] advises its use in endometritis. Tietze[125] also obtained good results in cases of pelvic infection and in his series were also three cases of endometrial hyperplasia: he thinks the optimal daily dose is 10,000 mouse-units. Tachezy,[126] however, claims clinical improvement following the use of much smaller doses in patients suffering from functional epimenorrhagia, and Runge[60] agrees that this form of bleeding is an indication for the use of oestrin. Ehrhardt[111] also quotes a case of pubescent haemorrhage which failed to respond to praehormone but was cured by intravenous injections of oestrin.

Goldstine and Fogelson[78] give details of a series treated with oestrin. They record 25 cures in 31 cases of functional uterine haemorrhage. However, none of their patients were young and most were approaching the menopause. Treatment was given for periods as long as one year and no fewer than 13 of the cures experienced permanent menopausal amenorrhoea during or after the treatment. In view of what has been said about the temporary nature of these diseases, these facts rather decry the significance of the bare statistics. However, a review of their cases reveals the fact that most patients did appear to have temporary relief from bleeding as a result of the treatment and even some of the younger ones subsequently developed short periods of amenorrhoea. The same authors report that all clinical types of bleeding respond equally well. Kaufmann[25] also notes the value of oestrin in menstrual irregularities at the menopause. However, Knab[6] and Allen[34] state that they were unable to obtain any improvement by using the follicular hormone, and Kurzrok, Wilson and Cassidy[88] not only failed to control haemorrhage by the administration of 40,000–100,000 rat-units of oestrin, but made the symptoms worse. Gerhardt[106] also noted no improvement following administration of 1,500 mouse-units of oestrin, yet he thinks this hormone is useful in some cases of menopausal haemorrhage. Guggisberg,[105] although he believes oestrin to be of some value, considers that gonadotropic or corpus luteum hormone therapy is more efficacious.

Oestrin therapy is practised in 13 of the foreign clinics replying to the questionnaire, but only Burger[P.5] reports good results: he uses an extract of pregnancy urine containing oestrin and ovipositor hormone and considers it more valuable, even in pubescent haemorrhage, than gonadotropic hormones. Kostmayer[P.22] limits its employment to patients of menopausal age, and prefers other endocrines for younger patients.

In spite of the comparatively few reports to the contrary, most observers consider the administration of oestrin either irrational or valueless. Nevertheless, consideration of various opinions leads to the conclusion that it may be indicated in the following cases:

(i) The rare cases of functional uterine haemorrhage which are associated with an atrophic endometrium (Martius[81]).

(ii) Ovulation haemorrhage which is due to a temporary and slight fall in blood-oestrin during the changing over from the oestrus to the luteal phase in the ovary (Runge[60]).

(iii) Excessive bleeding at the menopause which is not definitely of the metropathia haemorrhagica type.

Outside these indications, there appears no evidence to justify the use of oestrus-producing hormone in the face of the theoretical considerations outlined previously. In view of this no cases treated with oestrin are recorded from Liverpool, and no further discussion is included here.

Use of two or more Hormones in Combination.

(*a*) *Gonadotropic and Corpus Luteum Hormones.*

Theoretically this is ideal treatment since it is not only replacement therapy but provides for ovarian stimulation as well. No published statistics regarding its efficacy are available, but Latson,[95] Schenk,[94] Bishop, Cook and Hampson,[127] and Clauberg[109] all recommend it as being highly successful. Martius[81] also uses this technique for cases of pubescent haemorrhage in order to obtain both temporary and permanent effects. In view of what has been stated above, this treatment is more likely to control the haemorrhage than is the separate employment of one or other of the hormones, but it is doubtful if permanent correction of the menstrual disturbance will result.

(*b*). *Pregnancy Blood or Blood-serum.*

These substances contain the gonadotropic hormones, oestrin, and possible progestin, although this latter has, so far, not been demonstrated. The idea of giving blood from a pregnant woman (at about the sixteenth week of pregnancy) originates from the continent and is usually ascribed to Clauberg. There are no published statistics dealing with large numbers of cases, but individual successful cases are recorded. It is recommended by Witherspoon,[115] Goecke,[59] Damm,[121] Kane,[67] Siebke,[10] and Adair and Davis[P.1]. Two techniques are described:

(i) The administration of large quantities (400 c.c.) in a single intravenous injection: this method is especially useful if the patient is so anaemic as to require blood-transfusion.

(ii) The daily or frequent administration of small quantities (10 c.c.) intramuscularly. Damm[121] successfully used this latter technique in two patients whose bleeding had not been controlled by luteogan (Henning) or lutex (Leo). Miller, Salatich and Burch in his discussion on Novak's paper[42] all say that the method is valuable, but Miller and Salatich emphasize that transfusion of any blood may control uterine haemorrhage, so the results may have no connexion with the hormonal content of

the blood. This criticism is valid and it is impossible to assess what effect, if any, the hormones in the blood may have, nor is it possible to decide which particular hormone is responsible for the result. The method has a very limited application since it is difficult, even if desirable, to obtain quantities of blood from pregnant patients, and equally good results can be obtained with standardized preparations of luteum and luteinizing hormones.

(*c*). *Pregnancy Urine.*

This contains hormones similar to those of pregnancy blood. It was used occasionally before the preparation of potent extracts was possible. There are very few reported results of this method and such as there are, are quite encouraging. Schildberg[128] records two cases successfully treated by this means, and Kane[67] also mentions that it is useful. The employment of pregnancy urine has the same disadvantages as that of pregnancy blood. In addition, it is very difficult to sterilize the urine without destroying its hormones and, apart from the absence of expense, the method has very little to recommend it. Hormonic extracts, prepared from pregnancy urine, of which there are now several on the market, are more certain in their effects, and are to be preferred on both practical and aesthetic grounds.

FOR WHAT REASONS DO SOME CASES FAIL TO RESPOND TO TREATMENT WITH GONADOTROPIC AND CORPUS LUTEUM HORMONES?

It is at present impossible to account for all the failures in treatment, except on the grounds that our knowledge of the action of these hormones and of the cause of normal and pathological haemorrhage is incomplete. However, some of the failures experienced in practice are due to recognized causes, and some are avoidable.

1. *Faults in diagnosis.* It is certain that some cases regarded as failures show no response because an unrecognized gross pathological condition is present. Chronic inflammation of the appendages, a small fibromyoma, an intra-uterine polyp are diseases easily overlooked in an ordinary pelvic examination. Practically all writers recording a series of cases note this occurrence. A few examples of this kind, initially regarded as failures, are excluded from the Liverpool series, in view of the findings at subsequent laparotomy.

2. *Advanced stages of metropathia haemorrhagica.* Several observers (Holland,[129] Kaufmann[29]) note that endocrine treatment is of no avail if the follicular cyst in the ovary is unduly

large or the endometrium is so hyperplastic that large polypi are present. Three cases of metropathia haemorrhagica, which are included as failures in the Liverpool cases, had these findings. Nevertheless, some of the patients whose bleeding was controlled had cystic ovaries as large as a hen's egg: the cysts, however, remained palpably the same after treatment.

3. *Selection of cases.* From what has been said it is imperative, if the best results are to be obtained, that some effort is made to distinguish non-ovular from ovular bleeding. The complete investigations carried out at endocrinological clinics are not always practicable nor, in their present state, are they of much value except for research purposes. Estimation of the endocrine content of blood and urine is of no avail, with one exception, and that is the detection of the pituitary follicle-ripening hormone in menopausal cases. If the presence of this hormone is demonstrable by ordinary tests—as it is quite frequently in patients approaching the menopause—it is believed that treatment with gonadotropic hormones is useless (Anspach and Hoffmann,[130] Kane[67]). In only one of the menopausal patients here described was this hormone detected in the urine: she failed to respond to treatment. Estimation of the oestrin content of the blood and urine is of no significance: in metropathia haemorrhagica the amount of hormone in these fluids varies enormously. Thus Kane[67] believes that it is normal, Aschheim[131] and Albright and Halstead[132] think that it is increased, and Elden[120] notes that it is variable. Proust, Moricard and Rodier[133] demonstrated an abnormally large amount of oestrin in the blood and urine in one case. Frank[35] says that in metropathia haemorrhagica the blood oestrin is usually low and the urine oestrin high. Burch, Phelps and Wolfe[40] summarize the findings in this connexion and emphasize the extraordinary variation in the findings. The explanation depends naturally on the fact that metropathia haemorrhagica has two phases—the first when the blood oestrin is high, and a second, when bleeding commences, when the amount of oestrin is decreased. Hence any result may be obtained.

However, the one investigation which is simple to perform and makes it possible to diagnose at once whether a case is one of non-ovular haemorrhage and likely to respond to treatment, or whether it is of the ovular type and not so likely to respond, is an examination of the endometrium. This can be done without anaesthesia and with a minimum of discomfort to the patient by the employment of a suction curette to obtain material for micro-

scopic examination. This method is advocated by Swezy,[134] Campbell,[110] Anspach and Hoffmann,[135] Hisaw,[21] Klinger and Burch,[136] Smith,[137] Novak[33] and Rock,[138] all of whom regard it as the best method of estimating the nature and power of ovarian function. However, Frank[139] qualifies its usefulness by excluding negative findings. This method is now routinely practised by the author, and Novak's curette[140] fitted to the electric suction motor is used. It is, of course, unnecessary and impossible to carry out this procedure on young virgins, but in these the diagnosis of non-ovular haemorrhage can be made by a consideration of their symptoms and the probability of the occurrence of this type of bleeding in adolescence. Runge[60] agrees that the age and symptoms are reliable guides in the diagnosis in such cases. In married patients, however, whether they be nulliparous or multiparous, it can be performed with ease and is a valuable procedure. There is no doubt that the best published statistics are presented by observers who confirm the presence of non-ovular haemorrhage prior to the commencement of treatment.

4. ***Faults in technique.*** The activity of hormonic preparations, as supplied commercially, shows considerable variation, and, moreover, it deteriorates rapidly: this is particularly true of gonadotropic hormones. It is essential, therefore, to use preparations which are fresh, and if there is any doubt they should be tested biologically from time to time.

The route of administration appears to play some part in the results: most observers advise intramuscular injections: this technique was used in all the Liverpool cases. Nevertheless, Hisaw's work, in which it was shown that anterior pituitary extracts can produce luteinization in monkeys only if administered intravenously, has led many clinicians to adopt intravenous therapy. Zondek,[11] Clauberg,[109] Westman,[141] Sevringhaus, Campbell and Hisaw,[55] all state that this method is preferable. On the other hand Novak and Hurd[12] think that the intravenous administration of pregnancy urine extract has no special advantage over the intramuscular route. I myself have had only a limited experience of this technique and have used it only in cases in which intramuscular injections failed to control the bleeding. In all these instances intravenous administration was equally unsuccessful. Nevertheless, in cases of severe haemorrhage, or patients showing no response to intramuscular injections, intravenous therapy is to be recommended as worthy of trial.

The original dose of 100 to 200 rat-units of prolan given daily as suggested by Novak and Hurd[12] is still the general one, but

some workers, in particular continental ones, Martin,[8] Reiprick,[4] Westman,[84, 141] Runge,[3, 142] Goecke,[59] Dellipiane,[143] insist that better results are obtained with large doses, that is 1,000 to 2,000 rat-units daily. No large series of published cases in which this technique was used are available, but a study of individual case histories indicates that the response to massive doses appears to be only slightly better than those obtained with smaller amounts and they do not appear to justify such a liberal use of so expensive a preparation. Although the occasional use of a large amount of gonadotropic hormones should be tried in difficult cases, I believe with Allen[144] that the amount of hormone injected is of secondary importance and that persistence and continuity of treatment are the first essentials.

Finally, the periodicity of treatment. All writers insist that, unless the haemorrhage is cyclical in type, it is useless to inject hormones except when bleeding is in progress. Injections should then be given at least once in two days, or preferably daily. This is confirmed by the experience of Liverpool workers, and consideration of Table VIII reveals that the best results followed the daily injection, for the duration of haemorrhage, of 100 to 200 rat-units of hormone.

By what Mechanism is the Bleeding Controlled?

1. *Oestrin.*

This hormone, if effective, may bring about cessation of bleeding either by raising the level of the oestrin in the blood or by inhibition of pituitary, and hence follicular, activity. If its action is of this latter character, then oestrin therapy, theoretically, has a disadvantage in so far that it reduces the chances of future conception: Burger[P.5] emphasizes this point. Since the method is of doubtful value, its rationale questionable, and there are no reports on its effect on the ovaries and endometrium of patients treated for functional uterine haemorrhage by its means, it will receive no further consideration here.

2. *Corpus Luteum Hormone.*

Preparations of this hormone are now sufficiently potent to enable clinicians to produce a secretory phase in the endometrium. However, 35 to 50 Clauberg rabbit-units of progestin are required to produce a premenstrual reaction in patients suffering from secondary amenorrhoea (Kaufmann, Clauberg). Moreover, 100 to 200 Clauberg rabbit-units are required to trans-

form hyperplastic endometrium into a mucosa showing features of the progestational phase. This was shown by Kaufmann[25] and he quotes Butenandt and other workers who agree. It is, therefore, to be expected that any dose of progestin, other than a very large one, would be quite ineffective in controlling functional uterine haemorrhage. However, 10 rabbit-units, or even less, are usually sufficient, and it is, therefore, apparent that it does not control haemorrhage by creating a secretory phase in the endometrium. This is pointed out by Kaufmann[25] and has been confirmed in two recent cases in Liverpool by curettage immediately before and after successful treatment of bleeding. No histological differences in the curettings were noted. Westman[84] who uses 30 to 40 Clauberg rabbit-units of progestin in the treatment of functional uterine haemorrhage, thinks that *temporary* endometrial changes are produced, but all authorities are agreed that in the cases in which small doses of progestin are successful, the bleeding does not cease as the result of histological endometrial change. Corner[145] says it may "improve the condition of a deteriorated bleeding mucosa" or that there may be direct antagonism between the corpus luteum and follicular hormones. But such vague terms only serve to emphasize that the mystery is completely unsolved and that although large amounts of corpus luteum may control haemorrhage by bringing about an endometrial secretory phase, the prompt and brilliant results following administration of insignificant amounts is at present inexplicable. This problem was included in the questionnaire; four writers still think the response is due to an endometrial change, but one qualifies this by referring only to large doses, two attribute the results to an undefined restoration of hormonal balance, one (Knaus[P.20]) thinks it may cause rupture of the follicular cysts, but eight prefer to leave the question unanswered or state that the mechanism is unknown.

3. *Gonadotropic hormones.*

Here again the theoretical basis of treatment is sound but the mechanism of the action of these preparations is not determined. As with corpus luteum therapy, the problem is made difficult because the mechanism controlling the duration and amount of the bleeding in normal menstruation is unknown. The two questions are intimately connected, and the answer to one will probably lead to the explanation of the other. In this connexion it has recently been noted by Murphy, Shoemaker and Rea[146] that injections of gonadotropic hormones (antuitrin S)

are unable to affect in any way the character of the normal menstrual cycle. Although they should, gonadotropic hormones from pregnancy urine or placenta do *not* act by causing luteinization in the ovary, for:

(i) The bleeding ceases very quickly after their administration—long before it is possible for a corpus luteum to have formed. This was pointed out by the earliest workers, Novak and Hurd,[12] and has been confirmed by all authorities since.

(ii) The amount of hormone administered is quite inadequate, as calculated by effects in animals, to produce any gross ovarian response.

(iii) Many observers have examined the ovaries and endometrium after successful treatment and have failed to find any ovarian change or evidence of a secretory phase in the endometrium. In 18 of the Liverpool patients (five of whom were cured) the endometrium or uterus and ovaries were examined immediately after treatment. In no case was there any macroscopic or microscopic alteration in the ovaries or endometrium which could be attributed to the treatment. Follicular cysts remained unaffected. Klinger and Burch[136] also found no endometrial change in a successful case, and Burch and Burch[119] and Rock[138] record similar findings. Westman[141] could detect no ovarian change after prolan treatment. In spite of all the evidence to the contrary a few writers (e.g. Runge[60] and Gabrielianz[112]) still state that luteinization occurs.

(iv) There is grave doubt as to whether it is possible to produce luteinization in the human ovary even by massive doses of prolan preparations. Nevertheless, Zondek[11] claims to have produced small cysts in the ovary with such substances, and Mandelshtam and Chaykoviskiy[147] and Westman[84] observed naked-eye ovarian changes at laparotomy following the administration of prolan. Moreover, Geist injected antuitrin S into 50 mature women suffering from fibromyomata uteri and although, in his first communication,[100] he states there was no ovarian change, he subsequently[148] considers that follicular cysts and even luteinization were produced by this means. Hamblen, too, at first[149] was unable to detect ovarian response to subcuticular injections of small amounts of antuitrin S but, later,[150] describes even luteinization following its administration; even so, there was no corresponding endometrial change although he looked for it. The same workers refer to many others who have obtained similar results, and Meigs[68] from his

observations during laparotomies also infers that rapid luteinization may occur.

Yet all these experiments were uncontrolled and in the majority no attempt was made to examine the endometrium before and after treatment. A few writers (e.g. Hamblen[150]) note that in spite of apparent ovarian changes, gonadotropic hormones did not produce any secretory activity in the endometrium. This examination is far more important than is the study of the ovary since it can be controlled, and it provides an index of ovarian function which no histological examination of the ovary can supply. Furthermore, all investigations of this kind were carried out on patients in whom gross pelvic pathology justified laparotomy; only comparatively small amounts of prolan were injected and the ovarian examinations were often carried out many days or weeks after the treatment had ceased. In view of these obvious criticisms of the scanty evidence in favour of the artificial production of human corpora lutea, and the fact that corresponding endometrial responses did not occur or were not found, I believe that Corner,[145] in dealing with gonadotropic hormone administration, was completely justified when he wrote in 1935 that "evidence is totally lacking that the human ovary can be luteinized."

(v) It is impossible to produce ovulation, luteinization or premenstrual endometrium in immature or mature monkeys by means of pregnancy urine extracts (cf. anterior pituitary extracts) even when enormous doses are used, and are given intravenously (Hisaw, Fevold and Leonard,[22] Engle[16, 17, 19]). Johnson,[151] Ehrhardt,[111] and Engle[17] actually administered praehormone, antuitrin S, and similar preparations to monkeys, and after very heavy and continued dosage were unable to detect ovarian changes of any kind.

These remarks do not imply that anterior pituitary extracts are similarly ineffective. Engle[17] and Hisaw[21] showed that such substances can produce follicle-ripening if injected subcutaneously, in monkeys, and also luteinization at the edge of the follicles, if administered intravenously. However, they say that the production of lutein changes in cystic follicles is rare. Later, Engle[18] recorded the results of the administration of anterior pituitary hormone and prolan simultaneously to both immature and mature monkeys. By this means he produced normal corpora lutea. He concludes that prolan, given subcutaneously, inhibits the ovary or produces thecal luteinization. Anterior pituitary extract, however, can produce granulosa luteinization

and the two together, *if given intravenously* produce a normal corpus luteum. More recently Sevringhaus, Campbell and Hisaw[55] gave anterior pituitary extracts intravenously to the human subject and produced corpora lutea and a premenstrual endometrial reaction in four out of eight cases. In four of the failures they claim to have induced some early luteinization of cystic follicles: this is not in accord with the experience of Hisaw[21] who was unable to cause luteinization in cystic follicles in monkeys. These authors state that "we believe this is the first evidence of the production of corpora lutea in women by the use of anterior pituitary extracts."

These findings, if confirmed, should lead to the trial of combined treatment with anterior pituitary and pregnancy urine extracts for functional uterine haemorrhage and give promise of improvement in results.

However, if prolan does not bring about cessation of bleeding by corpus luteum production it would seem that it must act in one of the following ways:

(1) By affecting the platelet content or coagulation time of the blood. Although the work of Bablik[152] suggests that male sex hormone may affect the bleeding time, Geist and Spielman[153] have at least shown that antuitrin S has no effect on the blood elements.

(2) By "neutralizing" the "bleeding factor"—Novak and Hurd[12] originally suggested this at a time when a positive pituitary bleeding factor was postulated. As a result of the evidence recently reviewed by Engle, Smith and Sheleanyak[20] the idea of the existence of such a factor has been generally abandoned. Since bleeding is now regarded as representing a withdrawal phenomenon, this explanation of its control in these cases can hardly hold good. But Novak[35] still assumes some interaction between ovarian and gonadotropic hormones.

(3) By stimulating or assisting the anterior pituitary to bring about renewed follicular activitity in the ovaries and thus raise again the blood-level of oestrin—this has been suggested by Burch and Burch[119] on theoretical grounds only.

(4) By depressing the activity of the follicular apparatus either directly, as suggested by the investigations of Stockl,[154] Rock,[138] Hamblen and Ross,[155] and Engle,[18] or indirectly via pituitary inhibition as recorded by Leonard (quoted by Westman[84]), and Smith and Rock.[50] The latter observers noted in a case of menopausal haemorrhage that the follicle-ripening hormone, present in the urine prior to treatment, disappeared

subsequently to it. However, Wolfe[156] concludes from his experiments that pregnancy urine extract has no effect on the anterior pituitary of castrated rats.

(5) By exerting a direct effect on the uterus or endometrium. This is postulated by Burch and Burch[119] but there is no experimental or clinical evidence in its favour.

The following analysis of replies to the questionnaire sheds very little light on this mystery. Of 27 authorities, 14 refrain from expressing any views or state that the mode of action of gonadotropic hormones is unknown, three are content to go no further than to say that the hormonal balance is restored, four still believe it brings about luteinization in the ovary, and six imply an ovarian effect, possibly inhibition of follicular function either directly, or indirectly via the pituitary.

The main difficulty in accepting any of these suggestions is that they do not account for the rapid cessation of bleeding which takes place. Nevertheless, the recent experiments of Hisaw and Engle on monkeys and observations on the human being (*vide supra*) suggest that depression of follicular activity—evidenced by histological degenerative changes—is the most likely explanation. There is one clinical feature, noted previously, which strongly supports this contention, and that is the observation made by several independent workers, that during treatment with these hormones a temporary exacerbation of bleeding frequently occurs. This implies that the amount of oestrin in the body is further reduced by treatment—and this could be explained on the supposition that gonadotropic hormones inhibit the action of granulosa cells.

Treatment of Relapses—Antihormones.

References to the endocrine treatment of patients who have a return of haemorrhage after previous successful treatment are sparse, but reports of individual cases create the impression that the treatment is not nearly so successful when applied on a second occasion. Thus Henderson[65] reports only two successes in the treatment of five cases that relapsed. In the Liverpool series, 16 patients suffered a recurrence of symptoms and nine of these received further treatment with antuitrin S, but only five showed the good response which had been common to all initially. Two of the others were finally cured only by hysterectomy. This alteration in response to organotherapy may possibly be due to the development of hormonal antibodies as the result of the original treatment. This possibility was suggested by the work

of Bachman, Collip, Selye and Thomson,[157, 158, 159] Caldwell,[160] Hartman, Brownell and Crosby,[161] Twamley and Ferguson,[162] —in which the production of antibodies specific to anterior pituitary and pregnancy urine hormones was demonstrated. Experimental investigations of this kind are reviewed and criticized by Smith.[35] However, Fluhmann,[16] who confirmed the work of the above writers, found that the antibodies were not only specific for the particular substance injected, but were also species specific. He doubts whether these experiments have any clinical significance and emphasizes that there is no evidence of the production of antibodies to gonadotropic hormones, such as might be expected, during pregnancy in woman. Loeb and Friedman[164] found an adaptation in guinea-pigs to repeated injections of cattle's anterior pituitary gland, but noticed considerable variations in individual animals. There seems to be no doubt that some form of antibody or resistance can be produced by the injection of these substances, but Goldgerger[165] pointed out that the experiments might be explained by the presence of protein in the preparations, or by variations in the amount of the recipient's available pituitary hormone, or reactivity of the ovary.

Nevertheless, personal clinical experience certainly suggests that patients may become resistant to the treatment. In particular, one young girl complaining of pubescent haemorrhage was cured by injections of antuitrin S. Haemorrhage recurred one year later, and was uninfluenced by very large doses of the same preparation, administered both intramuscularly and intravenously. That this was possibly due to the formation of an antibody is evidenced by the fact that proluton was substituted for the antuitrin S and bleeding was controlled in four days by six clinical units. Wilson[166] records a somewhat similar case. In connexion with the question of antihormones a new line of treatment for functional uterine haemorrhage suggests itself, namely, the administration of oestrin antihormone. Unfortunately this is impossible, since this hormone differs from those of the thyroid, parathyroid, placenta and pituitary in that there is no evidence that its exhibition can produce any type of antibody (d'Amour, Dumont and Gustavson[167]).

Ill-effects of Treatment with Gonadotropic Hormones.

Local reaction at the site of subcuticular and intramuscular injections have been reported by several observers, but most are agreed they are not common. These cannot be blamed on faulty technique, since in the author's experience, although they are rare, they frequently occur in the same patient with each

injection. Their occurrence is possibly due to an antiseptic or preservative in the commercial extracts, and depends to some extent on the preparation used and the amount injected. Meigs[68] reports that local reactions to antophysin are common, Henderson[65] records some local reactions of a mild type to A.P.L. (Collip), but Novak and Hurd,[12] using the forerunner of antuitrin S, found it non-toxic and non-irritating. Martin[8] says he has seen no local ill-effects follow the use of prolan (I. G. Farben).

General reactions of the nature of syncope, fever, and generalized pains have also been the experience of some workers. Gabrielianz,[112] using a placental extract, had one patient who experienced faintness. Geist and Spielman[101] noted fever and generalized pains after the administration of large doses of antuitrin S. Smith and Rock[50] also record nausea and faintness coming on within 12 hours following 21 per cent of 412 injections of antuitrin S; they used doses of 2 c.c. to 10 c.c. Rosenblatt[168] and Laroche and Simmonet[169] also think that gonadotropic hormones can affect the patient adversely. But Westman,[141] Jarlow,[170] Martin,[8] Goecke,[59] all state specifically that they noted no general reaction, following administration of gonadotropic hormones.

Experience in Liverpool is limited to the use of antuitrin S in small doses (1 c.c. to 3 c.c.): reactions of any kind, either local or general, occurred on exceptionally few occasions, and these were so mild as to be almost negligible.

It may therefore be concluded that local and general reactions to most preparations of gonadotropic hormones occur but rarely, and their nature is such that they are insufficient to constitute a serious disadvantage.

There is one other possibility of which some workers (e.g. Gabrielianz,[112] Meigs[68]) are afraid: namely, that prolonged administration of gonadotropic hormones may permanently damage ovarian function, or may so over-stimulate follicular ripening and luteinization that sterility and premature menopause may ensue. From what has been said regarding the known effects of these hormones on the monkey and human ovary there can, at present, be no justification for such fears.

Conclusion.

The results presented in this paper may raise serious doubts even in the minds of those of us who are most ardent in the cause of endocrinology and its clinical applications. The

difficulties of organotherapy have long been realized and the recent tendency to regard its employment in cases of functional uterine haemorrhage as one of its few triumphs, has served to sustain faith in the conception of the important part it will ultimately play in gynaecological practice. It is, therefore, somewhat disconcerting to learn that its usefulness, even in this sphere, is strictly limited, and equally good, if not better, results are claimed, if not proved, for the use of oxytocic drugs, sea-kale, insulin, or even relatively impotent substances such as desiccated corpus luteum or unstandardized preparations containing very small amounts of follicular hormone.

Nevertheless, a more careful selection of patients, and continued attempts with improved technique based on sound endocrinological principles, will undoubtedly produce a considerable improvement in results in the hormonal treatment of functional uterine haemorrhage. The final complete success, however, will probably only be attained when the factors responsible for the control of the amount and duration of normal menstrual loss are elucidated, and when a liberal and cheap supply of hormonal preparations is available.

Summary.

1. An attempt is made to assess the value of the use of gonadotropic and ovarian hormones in the control of functional uterine haemorrhage. With this subject in view 80 cases are reported, those recorded in the literature are collected, and the opinions of foreign authorities incorporated.

2. This assessment is prefaced with an outline of the present-day views regarding the cause and types of functional uterine haemorrhage, and the rationale of treatment with the various hormones.

3. The following conclusions are reached:—

(*a*) The use of ovarian and gonadotropic hormones in the treatment of functional uterine haemorrhage does not produce the brilliant results which some authors have claimed for it.

(*b*) Until the present views and theories regarding the ability of oestrin to produce luteinization are confined or clarified, there is no theoretical basis for the administration of this hormone in the treatment of functional uterine haemorrhage, unless this bleeding be associated with endometrial atrophy, or represents merely a menopausal menstrual irregularity, or slight loss at the time of ovulation.

(*c*) The number of cases treated with corpus luteum is as yet too small to draw definite conclusions, but it would appear that the results obtained with it are as good as those accruing from the use of gonadotropic hormones.

(*d*) The type of bleeding showing the best response is that which is non-ovular in type, as in the condition known as metropathia haemorrhagica.

(*e*) Pubescent and adolescent haemorrhage is very amenable to the treatment, but menopausal haemorrhage shows very little response. Fortunately, it is the former type of case for which this conservative treatment is especially indicated, whereas for the latter more radical operative or radiological therapy is usually to be preferred.

(*f*) At puberty, the bleeding is controlled in 80 per cent of cases, but of all patients suffering from functional uterine haemorrhage only 66 per cent derive real benefit.

(*g*) The treatment controls the bleeding only temporarily: any subsequent amenorrhoea or return to normal cycle merely represents the ordinary probabilities of such cases. A return of haemorrhage is not infrequent and the hormonal treatment of the relapse is more difficult than that of the original bleeding.

4. Methods of improving the results are suggested.

5. The mechanism by which these endocrines exert their good effect is discussed.

6. Comment is also made on the possibility of the development of hormone antibodies.

7. Any ill-effects of treatment are considered rare and constitute no real disadvantage to the practice of organotherapy in these cases.

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EXPLANATORY REMARKS CONCERNING COMMERCIAL PREPARATIONS MENTIONED IN THIS PAPER.

AGOMENSIN, Ciba Ltd. Dispensed in ampoules and pellets containing "hydrosoluble ovarian substance" and said to be capable of inducing oestrus. Probably prepared from the ovary, and is not standardized.

ANTOPHYSIN, Winthrop Chemical Co. Gonadotropic hormone extract of pregnancy urine, marketed in ampoules containing 100 or 500 rabbit-units of soluble powder.

ANTUITRIN "S," Parke, Davis and Co. Gonadotropic hormone extract of pregnancy urine supplied in 10 c.c. vials containing 100 rabbit-units per c.c.

A.P.L., Ayerst, McKenna and Harrison. Gonadotropic hormone extract of placenta (Collip method). Dispensed in 5 c.c. vials containing 100 "biological day units" per c.c.

GLANDUANTIN. A preparation of anterior-pituitary-like hormone (? obtained from pregnancy urine). Used in Yugoslavia, but maker's name not available.

"LUTEINIZING HORMONE FROM PREGNANCY URINE." Used by earlier American workers, prepared by Parke, Davis and Co., and the forerunner of Antuitrin "S."

LUTEOGAN, Henning. A standardized solution in oil of corpus luteum hormone containing 1 Clauberg rabbit-unit per c.c.

LUTEOGLANDOL. Used in Austria and Germany: manufacturer's name not available. Prepared from corpora lutea, dispensed for oral administration, and probably contains small amounts of oestrus-producing principle.

LUTEX, Leo. Standardized preparation of corpus luteum hormone.

PRAEHORMONE, Promonta, Hamburg. Standardized preparation of gonadotropic hormones, *not* prepared from the anterior pituitary gland, and therefore derived either from placenta or pregnancy urine. Given intramuscularly and also in form of suppositories. The two original forms of praehormone, A and B respectively, are now replaced by one which is identical with the former praehormone B, 100 rabbit-units per c.c.

PREGNYL. Organon Laboratories. Gonadotropic substance from pregnancy urine. Supplied as water soluble powder in ampoules containing 30–100 rabbit-units each.

PROLAN. At least two commercial preparations bearing this name; I. G. Farben and Bayer Products both manufacture such a substance from pregnancy urine. Bayer's product is supplied in ampoules containing 100 rabbit-units soluble powder, also in the form of tablets.

PROLUTON, Schering, Ltd. Standardized corpus luteum hormone. Supplied in ampoules each containing two clinical units per c.c. Three clinical units equals one Clauberg rabbit-unit.

SISTOMENSIN, Ciba Ltd. Supplied in the form of tablets, or as a solution for parenteral use. Contains oestrus-producing principles, but activity is not expressed in any units. Was probably prepared initially from corpora lutea.

THEELIN, Parke, Davis and Co. Prepared from pregnancy urine, supplied in ampoules of either aqueous or oily solutions of crystalline ketohydroxoestrin. Each c.c. contains either 200 or 2,000 international units—varying with the solvent.

TABLE I.

Treatment with gonadotropic hormones.

Reference	No. of cases	No. of cures	No. improved	No. of failures	Percentage cured	Percentage improved	No. of relapses	Preparation used	Comments
Anspach and Hoffmann[54]	40	38	—	2	95	—	Several.	Luteinizing hormone from pregnancy urine. (Parke, Davis.)	Best results in adolescence. Results probably temporary.
Novak and Hurd[12]	51	44	—	7	86	—	Some.	Luteinizing hormone from pregnancy urine. (Parke, Davis.)	——
Campbell[110]	82	64	9	9	78	10	2	A.P.L. (Collip.)	Three failures had local disease.
Henderson[65]	39	25	6	8	64	15	5	A.P.L. (Collip.)	Four failures had local disease. Best results in menorrhagia.
Neumann[114]	7	7	—	—	100	—	Several.	Praehormone. (Promonta.)	All cases of non-ovular haemorrhage (probably). All cures probably temporary.
Ehrhardt[111]	3	2	—	1	66	—	—	Praehormone. (Promonta.)	All cases of pubescent haemorrhage.

TABLE I (*continued*).
Treatment with gonadotropic hormones.

Reference	No. of cases	No. of cures	No. improved	No. of failures	Percentage cured	Percentage improved	No. of relapses	Preparation used	Comments
Siebke[10]	34	29	—	5	85	—	—	Praehormone. (Promonta.)	All cases of pubescent haemorrhage with endometrial hyperplasia.
Meigs[68]	58	32	—	26	54	—	32	Antophysin.	Metrostaxis following amenorrhoea gives best results. All cures temporary.
Goezy[113]	46	22	13	11	50	28	22	Glanduantin.	Best results in pubescent haemorrhage. No cures menopause. Cyclical haemorrhage gives best response.
Martin[8]	13	12	—	1	92	—	—	Prolan. (I. G. Farben.)	———
Westman[84]	4	2	1	1	50	25	1	Prolan igefa.	Best results at puberty. The failure was a menopausal case.
Lawrence[116]	10	10	—	—	100	—	—	Not stated.	All pubescent cases. Some required intermittent treatment for two years.

TABLE I (*continued*).

Treatment with gonadotropic hormones.

Reference	No. of cases	No. of cures	No. improved	No. of failures	Percentage cured	Percentage improved	No. of relapses	Preparation used	Comments
Witherspoon[115]	8	8	—	—	100	—	—	Pregnancy blood.	Endometrial hyperplasia responds best.
Gabrielianz[112]	24	18	—	1	95	—	—	Placental extract.	Best results in epimenorrhoea. Five cases still treatment at time of report.
Elden[120]	7	7	—	—	100	—	1	Antuitrin "S" and desiccated anterior pituitary by mouth.	——
Geist and Spielman[100, 101]	28	8	5	15	28	18	3	Antuitrin "S".	Author very little impressed by method of treatment.
Smith and Rock[50]	56	28	22	6	50	39	—	Antuitrin "S".	Temporary cures only.
Liverpool results	79	50	14*	15	63	18	15	Antuitrin "S".	See Tables IV, V, VI.
Total	589	406	70	108	68.7	11	—	——	Five cases with treatment incomplete.

* Including cases with doubtful result.

TABLE II.

Treatment with corpus luteum hormone.

Reference	No. of cases	No. of cures	No. improved	No. of failures	Percentage cured	Percentage improved	No. of relapses	Preparation used	Comments
Knab[6]	8	7	—	1	87.5	—	1	Luteogan. (Henning.)	Bleeding of puberty responded best.
Kaufmann and Bickel[171]	16* (12)	8	1	3	75	8.3	1	Luteogan.	——
Kaute[108]	8	8	—	—	100	—	Several.	Luteogan.	Pubescent cases required more hormone and tended to relapse.
Scheidt[122]	6	6	—	—	100	—	—	Luteogan.	Probably all cases had non-ovular bleeding. None of menopausal age.
Westman[84]	9	3	2	4	33	28	2	Lutex (Leo) + prolan in two cases.	All menopausal or premenopausal.
Total	47	32	3	8	68.1	6.4	—	——	Treatment incomplete in four cases.

* Four patients refused to continue treatment although their bleeding still persisted.

TABLE III.

Treatment with Oestrin.

Reference	No. of cases	No. of cures	No. improved	No. of failures	% cured	Preparation used	Comments
Goldstine and Fogelstone[78]	31*	25	—	6	8.06	Placental extract	Two failures were found to have fibroid polypi
Hamblen[172]	6	2	—	4	33·3	Theelin, calcium and parathormone.	
Total ...	37	27	—	10	72.9		

* Nearly all patients were approaching menopause, treatment was continued for several months and 13 cured patients developed permanent climacteric amenorrhoea.

TABLE IV.

Treatment of pubescent haemorrhage with Antuitrin S (Liverpool cases).

Type of bleeding	No. of cases	No. cured	No. of failures	Improved or results doubtful	No. of relapses	% cured
Metrostaxis with or without preliminary amenorrhoea	14	11	1 Non-ov=1	2 Non-ov=1 Ov=1 C=2	4	78.5
Epimenorrhoea or epimenorrhagia	5	3 Non-ov=1	—	2	1	60.0
Menorrhagia ...	3	2	—	1 D.C.=1	1	66.6
Total	22	16	1	5	6	77·7

Four patients had at least one curettage previously and symptoms had recurred.

TABLE V.

Treatment of patients aged 20 to 40 years with Antuitrin S (Liverpool cases).

Type of bleeding	No. of cases	No. cured	No. of failures	Improved or results doubtful	No. of relapses	% cured
Metrostaxis with or without preliminary amenorrhoea	30	21 Non-ov=8 Ov=1 P=1	7 Non-ov=6 T=3 G.D.=2 Path=1	2 C=1 D.C.=1	8	70.0
Epimenorrhoea and epimenorrhagia	10	4 Non-ov=1 P=1	3 Ov=2	3 Ov=1 D.C.=1 P=1	1	40.0
Menorrhagia	8	4 Non-ov=1	1	3 Ov=1 T=1	2	50.0
Excessive bleeding at infrequent intervals	1	1 P=1	—	—	—	
Total	49	30	11	8	11	61.2

Twenty-two patients had had at least one curettage previously and symptoms had recurred.

TABLE VI.

Treatment of patients aged more than 40 years with Antuitrin S (Liverpool cases).

Type of bleeding	No. of cases	No. cured	No. of failures	Improved or results doubtful	No. of re-lapses	% cured
Metrostaxis with or without preliminary amenorrhoea	7	4 Non-ov = 3	3 Non-ov = 2	—	—	57.1
Menorrhagia	1	—	—	1 Ov = 1	—	—
Total	8	4	3	1	—	50.0

Six patients had had at least one curettage previously and symptoms had recurred.

KEY TO TABLES IV, V, VI.

Non-ov. = Non-ovular bleeding proved.
Ov. = Ovular bleeding proved.
P. = Became pregnant.
T. = Faulty technique.
D.C. = Delayed cure.
C. = Therapeutic curettage in addition to hormone therapy.
Path. = Other pathology, e.g. pelvic adhesions, present
G.D. = Large follicular cysts and endometrial polypi present

TABLE VII.

Details of times of observation of patients.

Result	Less than 3 mths.	3–6 mths.	6–12 mths.	1–2 yrs.	2–3 yrs.	More than 3 yrs.	Total
Cure	10	12	11	9	4	4	50
Failure	9*	1	1	4	—	—	15
Doubtful result or improved	—	3	4	4	3	3	14
Total	19	16	16	17	7	4	79

* All these patients received operative treatment when hormonal therapy failed.

TABLE VIII.

Dosage and technique.

Total amount	1–5 c.c.	6–10 c.c.	11–15 c.c.	16–20 c.c.	21–30 c.c.	31–60 c.c.	amount unknown
0.5 c.c. or 1.0 c.c. daily	C=9 F=1 D=2	C=11 F= 3 D= 1	C=3 F=1		C=1	F=1	C=1 F=1
2.0 c.c. daily ...		C=4 D=4*					
0.5 c.c. or 1.0 c.c. daily premenstrually and intramenstrually	D=1	C=1 F=1	C=3 F=1		C=1	C=1	C=1
0.5 c.c., 1.0 c.c., 2.0 c.c., three times weekly	C=2 F=2		C=1 D=1	C=2		C=1 D=1	
0.5 c.c. or 1.0 c.c. twice weekly	C=1 D=1	C=3 D=1	C=1		C=1		C=1 F=1
0.5 c.c. or 1.0 c.c. once weekly	C=1 F=1 D=1		D=1				
Irregularly		F=1	F=1				
Total	22	30	13	2	3	4	5

C=cured. F=failed. D=doubtful result or improved.

TABLE IX.

Reference	Preparation used			Results	Permanency of effects	Age giving best results or at which treatment is indicated	Type of bleeding showing best response
	Oestrin	Corpus luteum	Prolan				
Adair and Davies (P.1)	—	—	+	Variable	Variable	Puberty	———
Atlee (P.2)	—	—	+	33 per cent	(?) Permanent	All	M.H.
Dawson (P.10)	—	—	+	Variable	Permanent	Puberty	M.H.
Scott and Watson (P.36)	—	—	+	Good	(?) Permanent	Puberty; not menopause.	All
Fluhmann (P.16)	—	—	+	Good	Temporary	Puberty	All
Ward (P.43)	—	—	+	Variable	Variable	Puberty	M.H.
Cooke (P.7)	—	—	+	Poor	Temporary	Puberty	———
Danreuther (P.9)	—	—	+	Good	Variable	Puberty	All
Litzenberg (P.24) ...	—	—	+	Variable	Variable	Puberty	All
McLeod (P.30)	—	—	+	Good	50 per cent permanent.	Active sex life.	M.H.
Phaneuf (P.33)	—	—	+	Variable	Variable	All	M.H.
Plass (P.34)	—	—	+	Fair	Temporary	Puberty	———
Taylor (P.38)	—	—	+	Poor	Temporary	All	M.H.
MacKay (P.29)	—	—	+	55 per cent	Temporary	Puberty and menopause.	———
de Snoo (P.11)	—	+	+	Poor	Variable	Puberty	———

(M.H. = metropathia haemorrhagica, metrostaxis or non-ovular bleeding.)

TABLE IX (*continued*).

Reference	Preparation used			Results	Permanency of effects	Age giving best results or at which treatment is indicated	Type of bleeding showing best response
	Oestrin	Corpus luteum	Prolan				
Westman (P.44)	—	+	+	Variable with prolan; fair with corpus luteum.	Temporary	Puberty	———
Müller (P.28)	—	+	—	Good	Temporary	All	M.H.
Kovacs (P.23)	—	+	—	Poor	(?) Permanent	Puberty; not menopause.	M.H.
Orfila (P.31)	—	+	—	Variable	Temporary	All	M.H.
Wagner (P.42)	—	+	—	Good	(?) Permanent	All	All
Knaus (P.20)	—	+	—	Good	Temporary	All	M.H.
Martius (P.26)	+	+	—	Poor		Puberty; not menopause.	M.H.
Pamboukis (P.37) ...	+	—	—	Fair	Permanent	All	All
Kostmayer (P.22) ...	+ (menopause)	—	+ (puberty)	Variable	Variable	Puberty	———
Tew (P.39)	+	—	+	Poor	Temporary	All	———
Koenig (P.21)	+	—	+	Poor		Prefers other endocrines.	
Maguire (P.25)	+	—	+	Poor	———	Puberty	———
Heynemann (P.19) ...	+	++	+	Poor	Temporary	Maturity	M.H.

(M.H. = metropathia haemorrhagica, metrostaxis or non-ovular bleeding.)

TABLE IX (*continued*).

Reference	Corpus Preparation used: Oestrin	luteum	Prolan	Results	Permanency of effects	Age giving best results or at which treatment is indicated	Type of bleeding showing best response
Bogdanovitch (P.4) ...	+	+	+	Poor	Temporary	All	———
Stander (P.37)	+	+	+	Poor	Results all spontaneous.		
Villard (P.40)	+	+	+	Poor	Variable	———	———
Burger (P.5)	++	+	+	Good with oestrin; fair with prolan.	Permanent with oestrin; temporary with prolan.	Puberty	All
Runge (P.35)	+	+	+	Good with corpus luteum; fairly good with prolan.	———	All	Prolan in metropathia haemorrhagica; other hormones in cyclical bleeding.
Guggisberg (P.17) ...	±	++	+	Good with corpus luteum; variable with prolan.	———	All	———

Authorities not using organotherapy	5	Daels (P.12), Curtis (P.8), Essen-Moller (P.15), von Franque (P.41), Henkel (P.18).
Authorities using other forms of organotherapy	4	Ellul (P.13), Miller (P.27), Conill (P.6), Binet (P.3).
Authorities whose experience is small and results are so variable that no opinion is given	1	English (P.14).

TABLE X.

Summary of replies from foreign clinics=34.

Total number of replies 44
Clinics not using this form of organotherapy 10

Preparation used	Immediate results			Duration of effect			Type of bleeding for which use is restricted or preferred			Age of patients for which treatment is restricted or preferred				Number of clinics using preparation
	Good	Poor or fair	Variable	Temporary	Permanent	Variable	Metropathia haemorrhagica anovular bleeding, metrostaxis	Cyclical bleeding	All types	Puberty	Puberty and menopause	All ages	Menopause excluded	
Oestrin	1	9	3	3	2	2	2	1	2	3	—	6	1	13
Corpus luteum ...	5	8	2	6	(?) 2	2	5	1	2	4	—	8	1	15
Gonadotropic hormone	5	14	8	10	(?) 3	9	10	—	3	15	1	9	1	27

The Use of Radium in the Treatment of Benign Uterine Bleeding.

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the University of Liverpool.)

DURING the last 25 years radium has been used more and more in the treatment of benign uterine bleeding, and at the present time most gynaecological clinics would be in a position to produce an extensive series of cases. A forecast made by Lockyer[1] in 1914 is interesting and has certainly proved a true one. Discussing the recent developments in the X-ray and radium therapy of fibroids and carcinoma which had been made in France and Germany, he stated that the gynaecologist, who had started by being a physician and had already proved sufficiently adaptable to become a surgeon when surgery was required of him to fulfil his duties, must now similarly betake himself to the study of radiology. It would not indeed be far from the truth to say that at the present day radium finds a greater applicability to the treatment of benign bleeding than of malignant lesions.

The modern technique for the use of radium in the treatment of benign bleeding has developed out of its use in the treatment of fibroids. At the present time, however, fibroids occupy a place secondary to malfunctional bleeding among the indications for radium. For that matter the methods and results of the radium treatment of fibroids do not differ from those obtaining in the treatment of the other types of benign bleeding, subject to certain well-defined conditions which specially apply to fibroids. These conditions, first enunciated by Chéron[2] in 1909, are now generally accepted, and, subject to their recognition, the presence of a fibroid is merely an incidental factor when the question of the propriety of radium therapy is considered in a case of benign bleeding. Fibroids may, therefore, be best considered, not separately, but among the various other conditions which may limit the applicability of radium therapy.

Material of the Inquiry.

In Liverpool we have treated 432 cases of benign bleeding with radium, and 200 of these cases have been available for after-study. A mere enumeration of the results we have obtained would be, at the best, but a repetition of the many thorough studies already published. For this reason, and also in view of the very success of radium therapy, most attention is given in the present paper to its failures and complications, both those encountered personally and those recorded in the literature.

Supplementing our own findings 37 foreign clinics have contributed personal communications, placing us very much in their debt. Our thanks are also due to our colleagues in Liverpool who allowed their cases and methods to be incorporated in the inquiry.

Free use has been made of the many papers which have been published, notably those shown in the following list, which in the aggregate deal with 2,183 cases.

Table I.

Author	Year	No. of Cases
Blacker	1923	77
Dannreuther, W. T.	1932	109
Donaldson	1932	202
Forsdike	1926	200
Kelly, H. A.	1915	36
Martindale	1933	45
Martius, H.	1934	87
Murray, E. F.	1928	30
McIlroy	1934	55
Naujoks	1934	285
Peightal	1932	600
Phaneuf, L.	1934	150
Smith, W. S.	1932	111
Titus	1920	91
Ward, G. Gray	1932	309

The subject falls naturally into the following sections, which will be considered separately.

A. *The Use of Radium for the Production of Permanent Amenorrhoea.*

1. Technique and dosage.

2. Incidence of (*a*) failure to control bleeding; (*b*) radium

injuries; (*c*) menopausal symptoms; (*d*) post-irradiation carcinoma.

B. *The Use of Radium in the Treatment of Menorrhagia with Conservation of the Menstrual Function.*

1. Dosage. (Technique similar to that of Group A).

2. Incidence of (*a*) failures to control bleeding; (*b*) post-irradiation fibrosis; (*c*) impairment of the reproductive function.

C. *The Use of Radium in the Treatment of Post-menopausal Bleeding.*

D. *The Respective Scope of Radium and X-ray Therapy.*

E. *The Effects and Action of Radium on the Uterus and Ovaries.*

(This section is considered last because any conclusions which may be reached are based on the clinical experiments embodied in the earlier sections.)

A. Radium in the Production of Permanent Amenorrhoea.

Of our 200 cases 178 or 86 per cent fall into this category. Of these 7.5 per cent were between the ages of 51 and 55, 27 per cent between 45 and 50, 50 per cent between 41 and 45, 8.7 per cent between 36 and 40, 5 per cent between 31 and 35. Only one patient was under 30, a girl aged 29 suffering from mitral stenosis and intractable menorrhagia.

There were no cases of post-operative death in the whole series. There were four failures to control bleeding, a percentage of 2.2, although in three cases a secondary irradiation was necessary. These and other complications are discussed later.

1. *Technique and Dosage.*

In Table II, I have embodied the technique adopted by a representative series of observers who furnish personal communications. The table shows the close approximation of American and British practice, also the preference of Continental workers for the use of larger doses or for X-rays. At the end of the table are shown the reasons given by the chiefs of six clinics who avoid the use of radium.

TABLE II.

Methods of Clinics using Radium to produce Permanent Amenorrhoea (based on personal communications).

Reference	DOSAGE. Mgms. R.E.	Hours	Mgm. Hours	Screenage	Reservations and contra-indications	Failures.
American.						
P.1	100	20	2000	Pt. 1 mm.	Only near menopause. Infections, pelvic pathology.	Two secondary hysterectomies.
P.16	90	12	100–1500	Br. 1 mm.	Pedunculated fibroids, pelvic infection.	Occur.
P.35	—	—	1200–1800	Pt. 1 mm.	Pelvic infection, multiple or pedunculated myomata.	In two per cent of cases.
P.31	100	24	2400	Pt. 1 mm.	Pedunculated fibroids, large fibroids, pelvic infection.	None.
P.32	50	20	1000	Pt. 0.5 mm.	Not under 40 years, submucous fibroids, pelvic infection, intestine adherent to uterus.	
P.29	—	—	1500	—	Only near menopause, submucous fibroid, pelvic infection.	
P.33	—	—	1900	Pt. 1 mm.	Only near menopause, infection, pedunculated fibroids.	None.
P.26	—	—	—	—	Only near menopause, infection, submucous and large fibroids.	Occur.
P.27	80–100	12–36	1200–1800	Br. 1.5–2.0	Ovarian neoplasms, pelvic infection.	Occur.
P.7	75–100	—	1200–1800	Br. 1 mm. with 0.5 mm. Pt.	Adnexal disease, previous laparotomy.	None.

TABLE II (*continued*)

Reference	DOSAGE. Mgms. R.E.	Hours	Mgm. Hours	Screenage.	Reservation and contra-indications	Failures.
P.5	100	12	1200	Au. 2 mm.		Rare.
P.2	Emanation		2000 m.c.h.	Br. 1 mm. Ag. 0.5 mm.	Pelvic infection, endocervicitis.	Two cases needed hysterectomy for recurrent bleeding.
P.4	50–100	16–36	1600–1800	Br. 2 mm.	Only near menopause, pelvic infection, pedunculated or large fibroids.	In improperly selected cases.
P.24	75	24	1800	—	Submucous fibroids, pelvic infection.	Several, including haematometra.
P.20	100	12–18	1200–1800	Pt. 1.5 mm.	Doubtful diagnosis, large tumours, pelvic disease.	
P.11	100	15	1500	Pt. 2 mm.	Pelvic infection, pelvic pain.	
P.19	50–100	—	1200	Br.	Only near menopause.	
P.21	60	33½	2000	Pt. 1.5 mm.	Degenerating fibroids.	None.
P.25	20	168	3360	Pt. 0.5 mm.	Adnexal disease.	In some cases of submucous fibroids.
New Zealand.						
P.8	50	24	1200	Pt. 1.5 mm.	Only near menopause, infection.	
P.34	75–100	48	3600–4800	Au.	Pelvic infection.	Rare.
Continental.						
P.3	50	96	4800	Pt. 2 mm.	Only near menopause, pelvic infection.	In five per cent of cases.
P.22	90–100	20–22	1800–2000	Br. 1.3 mm.	Only near menopause.	None.

TABLE II (*continued*)

Reference	DOSAGE Mgms. R.E.	Hours	Mgm. Hours	Screenage	Reservation and contra-indications	Failures
P.13	50 (repeated in 14 days)	20	2000	Pt. 1 mm.	Rarely used. X-rays preferred.	None.
P.17	80–120	24–48	2000–9000	Ag. 1 mm. Fe. 3 mm.		
P.14	1800	20	3600	Pt. 1 mm.	Rarely used.	None.
P.23	70	24–48	1500–3200	Br. 1.3 mm.	Majority treated by X-rays.	In one case out of 12 an adenocarcinoma found later.
P.12	—	—	—	—	Prefers X-ray castration because of risk of infection.	
P.28	—	—	—	—	Only patients near menopause.	
P.9	—	—	—	—	Only patients near menopause, always combined with X-rays.	One in 20 because of mistaken diagnosis.

P—Personal Communication. Pt.—Platinum. Br.—Brass. Ag—Silver. Au.—Gold Fe.—Iron.

Clinics avoiding Use of Radium to Produce Amenorrhoea.

Clinic.	Surgeon.	Reasons for Avoidance.
Utrecht (P.30)	de Snoo	—
Upsala (P.36)	Westman	X-rays preferred
Genoa (P.15)	Henkel, M.	Fear of inflammatory reaction
Rome (P.6)	Conill	X-rays preferred
Lund (P.10)	Essen-Moller	Six cases of subsequent malignant degeneration led to abandoning of method.
Hungary (P.18)	Kovais	X-rays preferred because of risk of post-irradiation stenosis.

The technique which has been adopted in Liverpool, while it has been progressively modified as our experience has grown, does not differ essentially from most of the foregoing techniques. It may be summarized as follows:—

1. Exclusion of inflammatory disease of the appendages. The fact that no instance of pelvic inflammatory reaction has occurred severe enough to call for special comment or treatment, shows that either our selection of cases has been impeccable, or that the risks of causing a pelvic inflammation are small if flagrant cases of infection are excluded. In this regard the beneficial results obtained by Van de Velde,[3] Polak[4] and others in the treatment of gonorrhoea in women by means of a temporary radium amenorrhoea are significant. Naujoks[5] indeed gives tuberculous endometritis as a rare indication. The following case may be cited as an illustration of the problem.

One patient had had one ovary removed for inflammatory disease of the appendages. Menorrhagia and dysmenorrhoea ensued, but when hysterectomy was attempted two years later, it had to be abandoned because of the density of the adhesions present. A castrating dose of radium was then given without any inflammatory reaction ensuing, a complete symptomatic cure being effected.

2. Cases of fibroids in which the uterus is larger than it is at the twelfth week of pregnancy, cases in which the tumours are submucous or pedunculated, and cases in which the fibroids are degenerating and causing pain are excluded. Six of our patients had small fibroids which were regarded as merely incidental factors so far as the treatment was concerned.

The effect of radium on the cells of a fibroid is very small. In a fibroid of the cervix complicating a carcinoma a change was not observed one month after a massive dosage, totalling 6,000 mg.-hours.

3. Thorough curettage to exclude carcinoma.

4. The amount of radium used has varied between 30 and 50 mg. of the element. The hours of exposure have varied between 40 and 60 hours.

For the majority of cases a total dosage of 2,000 mg.-hours has been used, but larger doses, up to a maximum of 2,500 mg.-hours, have been adopted for women under 40 years of age.

In many cases, perhaps in a majority of the older women, such doses may have been unnecessarily large. Ill-effects were not found, however, to result from such a dosage, and in view of the occasional failures which do occur with smaller doses, the

additional assurance of success obtained makes a dosage of this magnitude desirable.

The consensus of gynaecological opinion shows that these amounts and times lie well within the limits of safety. Within these limits either factor, amount or time, may be varied in arriving at a desired dosage in mg.-hours without modification of the desired biological effect.

5. We have employed a filtration of 0.5 mm. of platinum, 1.2 mm. of silver, and 2 mm. of rubber. The range within which the filtration can be modified without causing alteration of results lies clinically between 0.5 ad 2 mm. of platinum, illustrated in Table II.

The curve[23] obtained by plotting the percentage of erythema-producing rays emanating from a given amount of radium under varying amounts of platinum screenage, shows a critical point when the thickness of platinum is 0.3 mm.; increase of screenage above this does not significantly modify the percentage of gamma rays emitted, the effect being merely to reduce the gamma-ray intensity out of all proportion to the small increase obtained in the percentage of the highly penetrating rays. For local applications, particularly in benign lesions when the specific cancer-effect is not desired, there does not appear to be any strong theoretical evidence for the use of very high filtration. Platinum 0.8 mm. or its equivalent appears to be a suitable thickness, both as regards the degree of filtration obtained and the important factor of the mechanical strength of the radium container.

6. Correlation between the length of the uterus and the length of the radium applicator.

In one of our cases the uterus measured five inches in length and this precaution was not observed. A second irradiation was required. In a personal communication J. B. Dawson[P.S] of Dunedin records a similar case, one of apparently true subinvolution, in which a secondary hysterectomy was required. The occurrence of such cases is some evidence that in a dosage sufficient to ensure permanent amenorrhoea the endometrial effect is of paramount importance.

7. Retention of the applicator *in situ* by means of thorough vaginal packing, paying special attention to the packing of the posterior fornix.

8. We have seldom found it necessary to employ an indwelling catheter. Despite the firm packing, retention of urine is very rare.

9. Routine periodic warning of the resident and nursing staffs of the precautions to be taken against the loss of radium.

2 (*a*) *The Incidence of Failure to Produce Amenorrhoea.*

There were four such cases, a percentage of 2.2. Their details are as follows:—

CASE 1, a 3-para, aged 41 years. Continued bleeding for two months. Intra-uterine radium, September 1931; 42 mg. × 42 hours = 1,764 mg.-hours. Amenorrhoea for six months, then menorrhagia for two months. Subtotal hysterectomy, June 1932.

CASE 2, a multipara, aged 32 years. Menorrhagia for four years. Intra-uterine radium, March 1931; 42 mg. R.E. × 36 hours = 1,512 mg.-hours. Amenorrhoea for five months, then return of menorrhagia. Subtotal hysterectomy, February 1932.

CASE 3, a 4-para, aged 36 years. Menorrhagia for two years. Intra-uterine radium, September 1930, 42 × 40 = 1,680 mg.-hours. Amenorrhoea for eight months, followed by return of normal periods.

CASE 4, a 3-para, aged 38 years. Menorrhagia for three years. Intra-uterine radium, June 1933, 42 × 40 = 1,960 mg.-hours. Amenorrhoea for eight months, then return of normal periods, followed by normal pregnancy February 1935.

In the first case the hysterectomy was, perhaps, premature. The possibility of irregular bleeding continuing up to 10 weeks, after even a massive intra-uterine dose, must always be borne in mind, and it is as well if patients are warned of this.

In our series a relation could not be established between this incidence of immediate bleeding and the time in the menstrual cycle at which the radium was inserted, although Runge[6] and others consider such a relation can be established in cases in which X-rays are used to produce amenorrhoea. It was noted, however, that the bleeding was commoner in cases in which the uterus was enlarged, or when endometrial hyperplasia had been noted.

The remaining three cases illustrate the need for the use of larger doses in women under 40 in whom permanent amenorrhoea is desired.

A transient late return of bleeding after one or two years of complete amenorrhoea is not a uncommon complication. We have had six such cases. In such an event the presence of a haematometra or a corporeal carcinoma must always be considered, but in each of our cases there has not been any secondary uterine enlargement, and the bleeding has ceased spontaneously. The fact that the bleeding was preceded and followed by a slight purulent discharge in three of the cases is in favour of the view that the cause is not always a recrudescence of ovarian activity but often a mild cervical or endometrial infection, pathologically akin to senile endometritis. In discussing this complication Forsdike[7] arrives at a similar conclusion.

2 (*b*). *The Incidence of Radium Injuries.*

The main step in the elimination of radium injuries was taken when the intra-uterine route of application was generally adopted. The development of a proper technique has further reduced these accidents to a negligible minimum. The absence in our series of any cases of persistent leucorrhoea, indicative of a radium burn of the cavity, may be attributed to the limitations of dosage already indicated, both as regards the amount of radium used and the hours of exposure. As in the case of the vulva, where radium effects can be more readily observed, the duration of tolerance of the connective tissues, and particularly of the blood-vessels, a tolerance which determines the incidence of radium burns appears to be under 70 hours.

2 (*c*). *The Incidence of Menopausal Symptoms.*

Only 23 per cent of the patients made a spontaneous complaint of menopausal flushing. This figure is rather lower than that given by Martindale,[8] who found an incidence of 36 per cent in cases of radio-therapeutic menopause as compared with 42 per cent after surgical castration and 20 per cent in the normal menopause. It is certainly clear that the radium menopause approximates more closely to the normal than that of the surgical.

Symptomatic mimicry of pregnancy, essentially a hormonal phenomenon, is not uncommon in cases of the radium menopause, particularly in younger women, and it may be quite difficult to convince the patients that these symptoms are not due to pregnancy. In one such case the Aschheim-Zondek test was positive three months later, in another the test gave a prolan A effect after two months.

Lassen and Brandstrup[9] have determined the amounts of urinary prolan after radiological and surgical castration. These authors used a method which showed the presence of prolan only when present in a concentration greater than 400 mouse-units per litre of urine. Their results may be summarized in the following table.

TABLE III.

	Prolan A present (percentage of cases)	Prolan B present (percentage of cases)
Normal menopause	13	14
X-ray menopause	30	7
Surgical menopause	50	9

The method of hormonal investigation may represent a possible mode of solution of the problem of whether radium acts

primarily on the ovaries or on the endometrium. Seeing that in the radium menopause the effect is usually immediate and these figures indicate a slow atrophy of the ovaries, the primary radium effect would appear to be endometrial.

2 (*d*). *The Incidence of Post-irradiation Carcinoma.*

This is perhaps the most important aspect of the subject. In a personal communication Essen-Möller[P.10] says he had six cases of corporeal carcinoma after radium castration and has accordingly abandoned the method. He considers the carcinoma may have been consequential upon the treatment. The danger is certainly very real. One such case occurs in this series.

A 2-para, aged 49 years, was given an intra-uterine application of 49 mg. R.E. × 40 hours = 1,960 mg.-hours. The uterus was three inches in length; thorough curettage and microscopic examination of the curettings did not reveal any malignant changes. Amenorrhoea ensued for 20 months. She then returned complaining of leucorrhoea which was occasionally blood-stained, and some vague colicky lower abdominal pains. The uterus was enlarged to the size of a 10 weeks' pregnancy. Secondary curettage did not detect any growth, but hysterectomy was performed and showed the uterine wall infiltrated by a columnar-celled carcinoma which the curette must have failed to reach. She died six months later with a rapidly growing recurrence in the iliac fossa and abdominal wall.

Martindale[8] records a case in which an adenocarcinoma developed one year after radium. Bland[10] records one significant case in which an early endometrial carcinoma was found three years after an intra-uterine dose of 2,400 mg.-hours. Schmitz[11] records two cases, occurring one and three years respectively after radium treatment of fibroids. Naujoks, recording one case after three years' amenorrhoea, states that each such case is of great theoretical and practical significance. He quotes three further cases (Koblanck,[12] Philipp,[13] Werner[14]). Leda J. Stacey[15] records two cases, one of fundal carcinoma appearing in a woman aged 55 after an intra-uterine dose of 600 mg.-hours, one a corporeal carcinoma appearing two and a half years after an intra-uterine dose of 500 mg.-hours for fibroids.

On the whole it seems likely that in most of these cases the carcinoma was already present at the time of the radium insertion. In the first place curettage, however thoroughly performed, is not infallible. In the second place, even in cases of known carcinoma of the body or of the cervix with corporeal involvement, there is often a free interval of several years before symptoms reappear. Finally, the rarity of post-irradiation carcinoma when curettage has been performed speaks against a causal relation between the two conditions.

If a carcinoma is unrecognized the real danger of radium therapy is that the productive fibrosis induced by the radium rays may so mark the growth that the onset of symptoms is deferred until a late stage of the disease is reached. The recurrence of a watery discharge together with secondary enlargement of the uterus should always be dealt with by immediate hysterectomy. To regard such a case as one of secondary haematometra or pyometra, would be unsafe, even if curettage failed to reveal any growth. In our cases no instance of either condition occurred although many have been recorded, e.g. Bland,[10] Mackay.[P.24]

B. *Cases in which Temporary Amenorrhoea or Control of Bleeding is desired.*

The value of radium in the temporary control of bleeding is a much more debatable question than that already considered.

Of the 32 clinics shown in Table II, the chiefs of which use radium to produce the menopause, only 12 favour its use in younger women, and the cases they treat are limited in number (Table IV).

TABLE IV.

Methods of Clinics Favouring Use of Radium to Control Bleeding.

Reference	Cases per year	Dosage (milligram-hours)	Subsequent pregnancy
P.16	Few	Maximum 750	No experience.
P.35	13	200–400	One normal. Malformations to be expected.
P.31	3	50 x 16 = 800	Normal.
P.32	1–2	300–400	Should be avoided.*
P.33	Rare	800	Normal.
P.7	10	300–750	Three normal, one abortion.
P.2	Rare	300 m.c.h.	No experience.
P.4	Rare	Preliminary dose of 75 to eliminate hypersentive cases. Later 150	———
P.20	Rare	50–100	No experience.
P.11	25 per cent of cases	600–800	Two normal pregnancies.
P.25	10.	1400	Normal. One case of cleft palate. (Coincidence?)
P.8	———	1200–4000	
P.3	Rare	400	One case, normal.
P.17	No longer		One case.

[Twenty clinics avoid the use of radium for this purpose.]

* Rarely of use in cases of simple bleeding in young women. Occasionally useful in cases of recurrent endometriosis.

Our own cases number only 15. They are shown in Table V. Their small number is due to the fact that recourse has not been made to radium until all other methods have failed. It will be seen that in seven cases the periods returned to a normal amount and frequency, in three cases the loss returned to normal but the interval increased, in two the periods continued heavy with an increased interval, in two an effect was not obtained, and in one the periods became scanty and irregular. While, on the whole, the results are satisfactory enough to justify the statement that there is a place for the use of radium in the control of bleeding, certain difficulties and objections must be considered, some of which certainly preclude the general adoption of the method.

1. *Dosage.*

This is intimately connected with the incidence of failure to control bleeding. In the Liverpool cases a close correlation could not be established between the results obtained and the dosage employed. This uncertainty of dosage is the main limitation of the method.

Our results would seem to show that radium increases the length of the cycle more readily than it modifies the amount lost at each period. Such a result suggests that the effect of submaximal doses is ovarian.

The only two calculable factors which modify the duration of the amenorrhoea induced are the age of the patient and her general health.

In every labour following the intra-uterine application of radium a dosage of 600 mg.-hours should not be exceeded except when conservation of menstrual function is not of paramount importance. A successful result would appear to depend upon whether the underlying causes of the menorrhagia abate during the period of amenorrhoea which precedes the return of the periods.

2. *Post-irradiation Fibrosis.*

In every labour following the intra-uterine application of radium the possibility of cervical scarring must be borne in mind. Its rarity, however, is demonstrated by the fact that in very few of the 402 pregnancies collected by Murphy[16] was any dystocia noted.

3. *Impairment of the Reproductive Function.*

This subject is certainly of outstanding academic interest. Among others Martius,[17] Parkes[18] and Bagg[19] have made notable contributions to the subject.

TABLE V.

Liverpool Cases in which Control of Bleeding was Desired.

No.	Age	Dose Mg.	Dose Hrs.	Mg.-hrs.	Previous history	Results
1	21	42	17½	735	D. and C. failed twice. General treatment failed.	Periods normal after five months amenorrhoea.
2	28	42	20	840	D. and C. failed twice. Hormonal treatment failed.	Normal periods after 10 months amenorrhoea.
3	35	46	42	1932	———	Amenorrhoea for eight months, then normal.
4	38	49	36	1764	———	Normal periods after 11 months amenorrhoea.
5	38	42	44	1848	D. and C. failed twice.	Normal periods after two months amenorrhoea.
6	35	42	14	588	———	Normal periods after three months amenorrhoea.
7	27	42	12	505	———	Three months amenorrhoea, then three to four days every 21–25.
8	19	42	8	336	D. and C. failed once. Hormones failed.	Variable but normal.
9	32	42	36	1512	———	Normal loss but irregular.
10	32	42	40	1960	———	Normal loss, interval increased, dysmenorrhoea not relieved.
11	22	42	15	550	———	Periods heavy, but interval increased.
12	35	40	20	800	D. and C. failed. Partial oöphorectomy failed.	Amenorrhoea for seven months, after two heavy periods, then heavy periods interval increased.
13	28	21	30	630	Mayo's operation failed. Ovaries fibrotic.	Amenorrhoea for four months, then heavy periods. Hysterectomy.
14	37	42	30	1260	D. and C. failed once.	Amenorrhoea for nine months, then return of menorrhagia, free interval of seven days only; pain not relieved. Hysterectomy.
15	36	42	30	1260	———	Periods irregular and scanty.

D. and C. = dilatation and curettage.

The fear of injury to the chromosomal constitution of the ovum by the use of radium is based on the known genetic mutations which can be induced in insects and lower animals by the use of very massive doses of pre-conceptional irradiation.

Bagg[19] in his paper published in 1924 makes the following statement, which has formed the basis of much clinical opinion. "In the treatment of menorrhagia in the childbearing age, we believe that complete sterility is preferable to the possibility of a damaged ovum, but such a conclusion is made entirely on the strength of experimental work on lower animals, and I do not feel justified in considering any of the available clinical records as adding conclusive evidence." Martius[17] similarly, on the basis mainly of the genetic mutations induced in Drosophila, states that, while the offspring of irradiated parents do not manifest any recognizable anomalies, he considers there may be some profound modification of the genotype which may manifest itself in a later generation.

On the other hand several observers, notably Matthews[20] and Murphy,[16, 21] who record in two papers a total of 600 children born after pre-conceptional maternal irradiation, have not observed any significantly higher incidence of foetal malformations. The total incidence of foetal malformations noted by Murphy was 11.6 per 1,000. The corresponding incidence of foetal malformations recorded by the author[22] in a series of 14,000 normal deliveries in Liverpool was 21 per 1,000.

Furthermore, foetal abnormalities and neonatal diseases have a complex aetiology, and to consider them all together is to fall into the error of confusion of categories.

It would appear that in man there is not any risk of foetal lesions following pre-conceptional maternal irradiation within the limits of dosage which we employ. The reaction of the oöcytes to radium is an all or nothing effect.

C. *Cases of Postmenopausal Bleeding.*

There were three such cases in the series. The need for exclusion of carcinoma is particularly important in this group. In one of the cases non-febrile pyometra was responsible for the bleeding. A dose of 2,000 mg.-hours, while it produced no inflammatory reaction, did not relieve the condition, and hysterectomy was performed later.

D. *The Respective Scope of Radium and X-Ray Therapy.*

In Liverpool we have in the main reserved the use of X-rays

for cases in which for some general reason curettage was impracticable or for patients suffering from cardiac disease or phthisis, when sterilization was desired. In such cases the method of fractional dosage has been adopted, using 220 KV.

The factors which have determined our preference for the use of radium have been that radium affords the opportunity for a confirmatory curettage, the greater assurance of permanent amenorrhoea, and the fact that one treatment only is required. The danger of corporeal carcinoma after the use of X-rays is certainly very much higher, shown for instance by Naujok's series of 58 cases.

E. *The Effects of Radium on the Uterus and Ovaries.*

Despite much inquiry the problem of whether the effects of intra-uterine radium are to be attributable primarily to its action on the endometrium or the ovaries still remains unsettled. Of 24 replies received in response to a *questionnaire* on the subject, 13 workers considered the ovarian effect to be dominant, four the endometrial, seven that the two effects were combined.

The problem is a typical instance of a common biological dilemma: to which of two reciprocal and simultaneous phenomena shall priority be given when the evidence can be interpreted equally well in either of two opposing ways? Such a consideration prevents any secure conclusions being drawn from the histological changes noted in the ovaries and endometrium after intra-uterine radiation. Animal experiments are unsatisfactory for two reasons, the definite variation in response to radium observed in different species, and the fact that experimental separation of the ovarian and endometrial effects possible in animals is impracticable in women, in whom both are always combined.

The following observations may be germane to the question. By the use of a castrating intra-uterine dose of radium a reasonably complete assurance can be given of a resultant permanent amenorrhoea. When, however, a single massive castrating dose of X-rays, the action of which is admittedly ovarian, is given, there is no such assurance of permanent amenorrhoea, hence the preference of most workers for the method of repeated dosage.

Hormonal studies similarly suggest that in the radium menopause the endometrial effect is predominant. Clinically the fact that menopausal symptoms are mild must be likewise attributed to the maintenance of some ovarian function. Matthews[20] specifically attributes this mitigation of symptoms to persistence of the

corpus luteum, the least susceptible to radiation of all the components of the ovary.

On the other hand, in cases in which radium is used merely to control bleeding, there is evidence that the ovarian effect predominates. The response in such cases to a given dose of radium is admittedly inconstant. The amount of radiation received by the endometrium can be measured within fairly precise limits, and the inconstancy of the results must be attributed to the operation of the variable ovarian factors which are present, the size, site and physiological condition of the ovaries.

The explanation of the problem may lie in a consideration of the two types of biological effect exerted by radium, its action on rapidly growing cells such as cancer and germ cells, and the general unspecific action it exerts in larger dosage on adult tissues, an action conditioned largely by their density and vascularity.

In the submaximal doses used when conservation of function is desired we are utilizing the selective effect of radium, mainly on the ripening oöcytes (Matthews) and the dosage is well below the threshold of irreparable reaction of the more resistant endometrium.

A castrating dose of radium on the other hand is over the threshold at which an irreparable endometrial effect is obtained, and what we, as a result of experience, regard as a minimal effective castrating dose, may be regarded as that level of dosage which ensures a permanent endometrial effect no matter what may be the amount of radiation by the ovaries.

Conclusions.

The present paper is essentially a summary of the results obtained by many workers. The satisfactory and probably permanent place of radium therapy in the treatment of benign bleeding at the menopause is confirmed and its technique discussed. Further consideration is given to the limitations governing the use of radium in women suffering from malfunctional bleeding in whom conservation of function as well as structure is desired.

Personal Communications (referred to in the text).

	Surgeon	Clinic
P.1	Adair, F. L.	University of Chicago.
P.2	Atlee, H. B.	V.G. Hospital, Halifax, Canada.
P.3	Binet, A.	University of Nancy.
P.4	Cook, W. R.	University of Texas.
P.5	Curtis, A. H.	New York.
P.6	Conill, V.	Barcelona.
P.7	Dannreuther, W. T.	Postgraduate Medical School, Columbia University.
P.8	Dawson, J. B.	Dunedin, New Zealand.
P.9	Daels, F.	University of Ghent.
P.10	Essen-Möller	Lund.
P.11	Emge, L. A.	Stanford University.
P.12	v. Franqué	Bonn.
P.13	Guggisberg	Berne.
P.14	Heynemann	University of Hamburg.
P.15	Henkel, M.	Jena.
P.16	Kostmayer, H. W.	Charity Hospital,
P.17	Koenig, R.	Geneva.
P.18	Kovais, A. F.	Hungary.
P.19	Litzenberg, J.	Minnesota.
P.20	McIlroy, L.	London.
P.21	Miller, N. F.	Michigan.
P.22	Mylks, G. W.	Kingston General Hospital.
P.23	Martius, H.	University of Göttingen.
P.24	Mackay, D. S.	Winnipeg General Hospital.
P.25	Müller, G.	Masaryk's University, Brno.
P.26	Orfila, J. P.	Montevideo.
P.27	Plass, E. D.	Iowa.
P.28	Phaneuf, L. E.	Carney Hospital Clinic.
P.29	Pamboukis, D.	Athens.
P.30	Stander, H. J.	Woman's Clinic, N.Y. Hospital.
P.31	de Snoo	Utrecht.
P.32	Scott, W. A.	University of Toronto.
P.33	Taylor, H. C.	Roosevelt Hospital, New York.
P.34	Tew, W. P.	Victoria Hospital, London.
P.35	Villard	Lyon.
P.36	Ward, G. Gray	Woman's Hospital, New York.
P.37	Westmann	Upsala.

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Case of Obstructed Labour caused by Cervical Fibroid undergoing Red Degeneration, and complicated by Placenta Praevia and Prolapse of the Foetal Cord

BY

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THE following case history seems worthy of record because of the unusual combination of abnormalities and because of the interesting operation specimen obtained.

Mrs. A. S., aged 39 years. Housewife. Previous pregnancies, five. The first four were easy labours, and the children are alive and well. At the fifth delivery the breech presented, and the child was born dead.

Present Pregnancy.

The date of her last menstrual period was uncertain, but it was thought that labour was due on 20th September, 1935. The patient had engaged a midwife, but an antenatal examination had not been made.

About 20th August, 1935, there was a slight, painless vaginal haemorrhage, which recurred on several occasions. The patient stated that she consulted her midwife and was told that such bleeding was not uncommon in the last month of pregnancy and need not cause any alarm. On September 8th, at 3.30 a.m., after abdominal pain (? labour pains) for one hour, a severe vaginal haemorrhage occurred. The midwife, who had already been summoned, now called in a doctor, who examined the patient at 4.30 a.m., and again at 11.30 a.m. As the result of this second examination the patient was sent to Fulham Hospital with the request that she should be admitted. Her doctor stated that a marginal placenta praevia, which he had previously felt, had now descended farther into the vagina, and that the presenting part was still high in the pelvis.

Condition on Admission.

On admission the patient was found to be in fairly good condition, although obviously suffering from loss of blood. There was a slight continuous bleeding from the vagina. She had been in labour for 12 hours.

On abdominal examination the foetus was found to be presenting by the vertex, with the head still above the pelvic brim. In the right iliac fossa there was a large, firm mass, which was thought by an experienced labour-ward sister to be the head of a second foetus.

A vaginal examination was made, and the following condition discovered. The foetal membranes were intact and filled the vagina. A prolapsed umbilical cord could be felt through the membranes: it was not pulsating. A portion of placental tissue projected from the uterus into the vagina. The cervix was situated at a very high level, and for this reason could only be felt in part; it was probably not more than a quarter dilated. On the right side, high up, there was a firm mass which filled the side of the pelvic brim and which was continuous with the tumour previously felt abdominally. It was evidently a cervical fibroid obstructing descent of the foetal head.

The patient thus presented an unusual problem. The placenta praevia and the continuing loss of blood demanded immediate treatment. At least five vaginal examinations had already been made, and septic infection was, therefore, almost inevitable. The fibroid precluded any possibility of delivering the child *per vaginam*. Clearly, abdominal delivery and hysterectomy were indicated. Since the foetus was dead, it seemed reasonable to remove the uterus intact, in order to avoid unnecessary soiling of the peritoneal cavity and also to lessen the amount of blood lost and shock. The patient was transferred to Hammersmith Hospital and laparotomy performed forthwith.

Operation.

Anaesthesia was induced with nitrous-oxide, oxygen, and ether.

Hysterectomy of the gravid uterus presented little difficulty. Before removing the organ, great care was taken to push down the bladder and ureters from the lower portion of the uterus; the lower uterine segment was then cut across just above its insertion into the vagina. (Caution was necessary at this stage, because the lax vagina of pregnancy allowed the uterus to be pulled up to a surprisingly high level, and the bladder and ureters were consequently exposed to unusual danger from carelessly applied clamps. Similarly, the mesentery of the pelvic colon was drawn dangerously near to the operation area and liable to injury during clamping of the infundibulo-pelvic ligament.) The fibroid was situated low in the right side of the cervix, and it was easily

enucleated from the broad ligament. In cutting across the uterus the foetal membranes were (for the first time) ruptured, and a small amount of liquor amnii escaped into the operation area. The vaginal opening was partially closed, and the raw areas peritonized in the usual fashion. A rolled-up piece of corrugated rubber was inserted into the pelvis and brought out at the lower end of the abdominal wound as a drain.

Apart from some difficulty with the anaesthetic, due to excessive mucous secretion, the patient stood the operation well, and returned to bed in good condition.

Convalescence.

During the first six days of convalescence the patient's temperature ranged around 101°F., and the pulse-rate varied from 110 to 120. In spite of this, her general condition was good. The abdominal wound healed by first intention. There was a moderate blood-stained discharge from the drainage opening for two or three days, but this soon ceased. The drainage-tube was shortened on the third day and removed on the fifth day. After the sixth day the temperature remained well below 100°F. and the patient appeared to be progressing satisfactorily. On the fourteenth day, however, she developed a sudden severe pain in the left side of the chest, and the temperature rose to 102°F. Pulmonary infarction was diagnosed. Cough, shortness of breath, and pleuritic pain were now very troublesome, and the pyrexia was sustained. After some weeks an empyema was suspected, and the patient was transferred to the surgical wards. On 8th October Mr. Harnett resected a rib on the left side, and discovered an inter-lobar empyema containing much dark-coloured, foul-smelling pus. The cavity was drained, but for some days the patient remained in a very critical state, profoundly toxic and very dyspnoeic. She later rallied, and her general condition improved greatly. On 21st December it was decided that drainage from the empyema was insufficient, and a further exploration of the pleural cavity was made. Drainage still proved inadequate, and radiological examination after lipiodol injection now showed that there was a bronchial fistula. On January 14th a further portion of rib was resected by Professor Gask, and the empyema cavity widely opened. From this operation the patient made a slow but complete recovery.

On 18th May the patient was re-examined. She was then in excellent health. Pelvic examination showed a supple scar in the vault of the vagina. There was no tenderness or induration. The

empyema wound was closed, and the scar was not causing any inconvenience.

Operation Specimen.

The operation specimen was hardened by injecting formalin into the substance of the organ at various parts and immersing in formalin solution for several months. It was then opened in coronal section. It showed:

(1) A large cervical fibroid measuring 6 inches by 5 inches by $4\frac{1}{2}$ inches and undergoing red degeneration.

(2) The placenta covering a large area of the posterior wall of the uterus and projecting about $1\frac{1}{2}$ inches into the vagina.

(3) Prolapse of the umbilical cord.

Figs. 1, 2 and 3 clearly illustrate the points of interest.

I acknowledge with thanks the assistance of the Medical Superintendents of Fulham and Hammersmith Hospitals (L.C.C.) for the arrangements made for the treatment of this case.

The history of the case is published with permission of the Chief Medical Officer of the London County Council.

FIG. 1.

The anterior half of the uterus, showing the foetus *in situ*, and the moulding caused by the cervical fibroid. The placenta projects $1\frac{1}{2}$" beyond the cervix, and there is a prolapse of the umbilical cord.

FIG. 2.

The posterior half of the uterus with the foetus placed in position.

FIG. 3.

The anterior half of the uterus. The placenta extends from the fundus to a point 1½" beyond the cervix. The fibroid is undergoing red degeneration.

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The Treatment of Uterine Haemorrhage in Non-Malignant Disease ; with special reference to the Choice of Surgical Operation versus Irradiation by Radium or X-Rays.

BY

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IN presenting this clinical study of the treatment of uterine haemorrhage in non-malignant disease, illustrated by a series of my own cases, I have been actuated by the hope that this Congress* would formulate a definite pronouncement for the guidance of medical public opinion on the value of conservative methods of treatment, assigning to each method its rightful place.

With the recent widespread distribution of radium in our country, and the comparative ease with which radium can be applied, there is all the more need that the associated dangers and contra-indications should also be widely understood, and that its use should be restricted to certain cases only. Again, the simplicity of the treatment has, for the moment, relegated to the background the deep X-ray therapy, which I hope to show is, in an even larger percentage of cases, a safer and more efficacious method of treatment if carried out by modern adequately standardized methods.

In deciding upon the best type of treatment for each individual case it is of primary importance—

(1) To diagnose the cause of the haemorrhage and the physical signs present.

(2) To know the age and civil state of the patient, and the degree to which future capacity for childbearing is important to her.

(3) To have in hand a full report of her general health.

I. *The Cause of the Haemorrhage.*

I do not propose in this short paper to enumerate all the causes which may lead to severe uterine haemorrhage; e.g. the various endocrine disturbances, the chronic pelvic inflammatory

* Congress of Obstetricians and Gynaecologists, Belfast, 1936.

diseases preventing normal muscular contraction of the uterus, the chronic inflammation of the endometrium resulting from puerperal sepsis, incomplete abortion, or gonorrhoea, or the haemorrhage following the presence of ovarian tumours, especially if torsion has taken place; nor of the metrorrhagia occurring during pregnancy as the result of placenta praevia, hydatidiform mole; or retained products of conception; but to confine myself to:

(*a*) *Metropathia haemorrhagica*—that hypertrophy and hyperplasia of the endometrium, the result of true hypertrophy in which the thickened endometrium is thrown into irregular folds, which assume a polypoid appearance, a condition known as "polypoid gland hypertrophy", or non-malignant adenoma of uterus (incidentally a condition not curable by curetting).

(*b*) *Uterine myomata*—in which the most severe form of haemorrhage is seen, associated with submucous fibroids.

(*c*) *Functional, idiopathic, or essential uterine haemorrhage*—that form of bleeding in which there is not any demonstrable pelvic disease; a form common at puberty and at the menopause, and more menorrhagic than metrorrhagic in character.

The *physical signs* are of great importance, a very careful examination of all the pelvic organs is, therefore, necessary. The size of a fibroid uterus and the consistence of the tumour noted, and an X-ray examination should be made if calcification of a fibroid is suspected.

If there is any doubt as to the non-malignancy of the condition, a biopsy, or diagnostic dilatation and curetting is performed. The possible presence of a pregnancy should not be forgotten, and a Zondek-Aschheim test is of great value.

II. *The Age of the Patient, her Civil State, and her Desire for Future Child-bearing.*

These are important factors. If grouped according to age, the following headings have been adhered to: (1) Adolescent, (2) child-bearing, (3) menopausal, (4) post-menopausal.

III. *The General Condition and Health of the Patient.*

This has to be carefully considered. A blood-count is necessary in almost every case to decide on the degree of anaemia present. The renal function, the respiratory, circulatory, and nervous systems, and the state of the ductless glands have also to be considered.

Choice of Treatment.

The three main types of treatment are: (1) Surgical operation, (2) radium, (3) X-rays. According to the literature the percentage treated by each of these methods differs widely, depending upon the nationality and practice of individual gynaecologists.

Surgical Operation.

Under operation one includes (1) diagnostic and therapeutic dilatation and curetting; (2) vaginal myomectomy, for submucous fibroids, removal of cervical polypi, and placental polypi; (3) abdominal myomectomy; (4) subtotal hysterectomy; (5) total hysterectomy.

In a small number of cases (according to Busse 10 per cent in 500 cases) dilatation and curetting will result in a cure. The removal of a pedunculated submucous fibroid by vaginal myomectomy with or without necrotic degeneration, is sufficient to cure the haemorrhage in another small percentage of cases. There remains, however, the large number of cases of hyperplasia of the endometrium, associated with or without fibromyomata of the uterus, in which more drastic treatment is necessary.

Briefly, the indications for abdominal myomectomy or hysterectomy are these: (1) The presence of a fibroid uterus larger than the size of a four months' pregnancy; (2) rapid increase in the size of the tumour, suggesting sarcomatous or benign degeneration; (3) a pedunculated fibroid even if the uterus is small; (4) necrobiosis, calcification or other degeneration of a fibroid proved or suspected; (5) pressure symptoms; (6) pain, this suggests additional lesions; (7) the co-existence of a pregnancy; (8) metrorrhagia with possible malignant degeneration of the endometrium or fibroid; (9) metrorrhagia with possible neoplasm of ovary or Fallopian tube.

In all these cases abdominal operation is indicated. When an abdominal myomectomy can be performed this is an ideal operation, for the patient can then look forward to the chance of a future satisfactory pregnancy should she desire it.

In my own series of cases (Table I) the percentage of cases so treated by surgical operation is 54. Many surgeons, however, report a higher percentage, although working in a clinic where both X-ray and radium therapy are available. In any case the percentage of cases best treated by operation is a

TABLE I.

Method of treatment in 762 cases of metropathia haemorrhagica, fibrosis uteri and fibromyomata.

Treatment	No. of cases	Per cent cases	Mortality per cent
Surgical operation	412	54.07	1.9
Irradiation (X-ray therapy 280, 36.74%; radium treatment, 70, 9.19%)	350	45.93	0
Total	762		

high one; (1) Polak, 77 per cent (906 cases treated); (2) Neill, of Baltimore, reports 75 per cent of his fibroid cases as being best treated by operation; (3) Martindale, 54 per cent (762 cases treated); (4) P. Werner, 50 per cent; (5) Gal, 45 per cent; (6) Zweifel ((Doederlein), 21 per cent; (7) Seitz and Wintz, 16 per cent.

The chief advantages of a surgical operation, whether it be the more conservative operation of myomectomy or the more drastic one of hysterectomy, are: (1) The possibility of really accurate diagnosis, macroscopic or miscroscopic, of the condition of the uterus, ovaries, and Fallopian tubes; (2) the postponement of all menopausal symptoms until the natural menopause occurs (except in those few cases in which bilateral oöphorectomy has to be performed).

Table II shows my own choice of the various types of operation performed and the results. The disadvantages of operation are: (1) The mortality varying from one to three per cent according to the type of operation and the general condition of the patient. (2) The discomfort and pain, and the occasional complications, associated with an abdominal operation, such as pulmonary infarcts, thrombosis, and sepsis. (3) The length of time spent in nursing home or hospital and for subsequent convalescence, varying on an average between six weeks and four months. (4) And in the case of the major operation the psychological effect on the patient of the loss of an important organ such as the uterus.

IRRADIATION.

Irradiation can be carried out by means of radium or deep X-ray therapy.

TABLE II.

End results in 412 cases treated by surgical operation.

	No. of cases	Died	Cases complicated by			
			Carcinoma	Sarcoma	Malignancy of other pelvic organs	Pregnancy
Subtotal hysterectomy only	179					
Subtotal hysterectory and oöphorectomy	92	2	2	2	2	
Subtotal hysterectomy and bilateral oöphorectomy	25				1	
Total hysterectomy only	29					
Total hysterectomy and oöphorectomy	13	1	6	2		
Total hysterectomy and bilateral oöphorectomy	7					
Abdominal myomectomy	33	4				2
Abdominal myomectomy and oöphorectomy ...	13					
Vaginal myomectomy ...	21	1				2
Totals	412	8	8	4	3	4

Radium Therapy.

Technique. Under anaesthesia a careful vaginal examination is made, the cervical canal is dilated up to No. 9 Hegar, and a diagnostic curetting performed. The uterine cavity having been measured, 50 mg. of radium element (or 30 mg. of radium element in a small uterus), are then inserted into the uterine cavity, screened by 1 mm. of platinum (the platinum or equivalent in lead, silver, or brass) is necessary to absorb the beta and soft gamma rays, which have a caustic effect on the endometrium with resultant radio-necrosis, retarding healing, and causing subsequent scarring with increased incidence of post-radiation pyometra), and 1.5 mm. of rubber (the rubber to filter out the secondary beta rays given off from the metal capsule itself; it also increases the distance). The empty cuff of th rubber tube, which has been cut to correspond with the entire length of the uterine cavity, occupies the cervical canal. It is hoped in this way to prevent any subsequent cervical stenosis. A pack of gauze wrung out of 1–4,000 acriflavine is then inserted into the vagina.

If an interstitial myoma is diagnosed a slightly larger dose is given, but it is generally found to be better to give the standardized dose of 50 mg. of radium element, and repeat it later if necessary.

Patients respond very variably to radium, and quite a small dose will occasionally lead to an unwanted permanent amenorrhoea. The length of time the radium is left *in situ* varies according to the age of the patient and the local condition: In adolescents under 18 six hours is sufficient, viz. 300 mg. element hours; in patients in the child-bearing age 12 to 14 hours, viz. 600–700 mg. element hours; in patients at the menopause 20 to 24 hours, viz. 1,000–2,000 mg. element hours. The aim in the first two groups is to check the menorrhagia without disturbing function; in the last group to produce an artificial menopause.

TABLE III.

Fifty cases treated with radium therapy, 1926–1934.

Classification of cases	No. of cases	Average dose m.e.h.	Cured	Not cured	Not traced	Subsequent treatment	% cured
Adolescent.							
Ages 16 to 19	3	300	3				
Childbearing							
age 20 to 40	8	866	5	3		Deep X-ray therapy, 3 cases cured	
Menopausal.							
Ages 41 to 55	33	1140	29	2	2	1 hysterectomy for carcinoma of fundus 1 year after; died later	
Post-menopausal.							
Ages 56 to 71	6	1458	4	1	1	Deep X-ray therapy, 1	
Totals ...	50		41	6	3		82

Table III.

Of the 70 cases I have treated by this method 50 are reported treated before 1934. From this it will be seen that 41 were cured, four had to have in addition X-ray therapy before the cure was complete, and in one case hysterectomy one year after for carcinoma of fundus.

In the last report of the Medical Research Council, the Marie Curie Hospital reports 833 cases of non-malignant haemorrhage treated in this way. Of these 549 cases have been followed up from one to six years. Of the 12 adolescent cases, 11 well, one improved; 136 child-bearing age, 117 well, 7 improved (14 no result); 399 menopausal cases, 384 well, 15 improved (viz. 93.2 per cent well).

In the number of younger patients there was irregular haemorrhage for two to three months followed by amenorrhoea before the menstrual periods became normal. In a few cases, all having had doses of under 750 mg. element hours, the amenorrhoea has persisted during the three or four years they have been under observation.

In the adolescent cases improvement was slow, and in some; although the haemorrhage has been cured, periods are irregular.

This method of treatment of fibroids and climacteric haemorrhage is popular in America, but is not much used in Germany, France, or Sweden, in which countries X-ray therapy is preferred.

The advantages of radium treatment over surgical are briefly the following: (1) Conservation of the uterus and ovaries and in many cases also of their function; (2) short duration in nursing home or hospital, and short convalescence.

Among the disadvantages Graves notes the unpleasant symptoms following radium treatment as being "nausea, continuance or reappearance of the bleeding, leucorrhoea, pain, acute nephritis, and nervous symptoms." The troublesome leucorrhoea following radium treatment is known by the Germans as Bestrahlungs-endometritis.

Also the mortality, according to W. Müller, was 2 per cent in a series of 103 cases of fibroids. Other authors quote mortality rates of between 0.3 per cent and 2 per cent, notably Petit-Dutaill's, Schmitz, Cleland, Bundy and Béclère, and v. Seuffert, who describe deaths following radium treatment as due to acute peritonitis or acute purulent salpingitis. The danger is greater in the case of fibroids than hyperplasia of the endometrium, especially in cases in which there are submucous polypoid myomata which become eroded and bleed, or undergo suppuration and gangrene.

Another disadvantage of radium treatment is the possibility of a future pregnancy, and the effect of the radium in causing stenosis of the cervix and so obstructed labour, and of the direct effect of the radium on the foetus *in utero*.

C. C. Anderson records a case of a married woman, aged 35 years, who was given 1,080 mg. element hours radium for uterine haemorrhage. Three years later she became pregnant, had an obstructed labour and a dead foetus, for which Caesarean section had to be performed.

In a more recent case, reported by Basden and Hurdon, a multipara, aged 33 years, was treated with 50 mg. of radium (intra-uterine) for 24 hours, in January 1932, for a sudden haemorrhage; the biopsy done at the time showed squamous carcinoma. She was allowed to go home for a week but, as the haemorrhage stopped, she did not return. The total dose of 1,200 mg. element hours was sufficient to keep the cancer quiescent for three years. In March 1934 she was admitted into hospital after having been in labour two days; she had a rigid stenosed cervix due to the radium treatment, for which Caesarean hysterectomy was the only possible treatment. In this case the radium treatment had been followed by temporary amenorrhoea lasting one year.

There are now records of many hundreds of cases of pregnancy following irradiation for non-malignant conditions, and a study has been made of the effect of pre-conceptional irradiation on pregnancy and parturition, and on the physical and mental development of the child. The chief anatomical defect observed in the offspring of patients subject during pregnancy to irradiation of the uterus and ovaries, has been microcephalic idiocy, but so far it has not been proved that this ever follows pre-conceptional irradiation.

Pregnancy following pre-conceptional irradiation for hyperplasia of the endometrium or fibroids, with a few exceptions, proceeds normally, and parturition is usually normal, according to Flaskamp and Murphy. Should a stenosed fibrotic cervix cause obstruction Caesarean hysterectomy must be performed.

Deep X-ray Therapy.

In deep X-ray therapy we have a form of irradiation which one may consider a specific in all forms of non-malignant haemorrhage due to metropathia haemorrhagica or small interstitial fibroids. The technique has undergone various modifications depending on the development of higher voltages, better X-ray tubes, and an experience of irradiation in many thousands of cases. With standardized calibration of the apparatus one treatment of 64 to 72 minutes is sufficient; this is followed by one, or at most two, monthly periods before the onset

of amenorrhoea of about two years in patients under 40, and is permanent in those over the age of 43.

I work at a voltage of 186,000 with four fields or ports of entry 8 by 10 cm., or two large fields; a focal distance of from 30 to 50 cm., and a filter of 0.5 Cu to 2 mm. Al. The patient has to be very carefully prepared; she should enter a nursing home the night before, and be prepared as for operation; a blood-count should be made, and the urine tested. The next morning she should be allowed only a light breakfast of tea and toast, and after the treatment should keep in bed for two or three following days.

Table IV.

The results are shown in Table IV. In the 280 cases treated by this method, 59 were under and 221 patients were over 40 years of age. In my earlier cases I treated a larger percentage with X-rays than with operation, and did not confine myself to a fibroid uterus smaller than that of a four months' pregnancy. Consequently my percentage of cures was less, and in 10 patients I decided later to perform a hysterectomy. In several of these cases, however, I found that this was really unnecessary.

With the more restricted choice of X-ray therapy which it is now my habit to make (viz. 46 per cent) the percentage of cures is greater. In Table V I chose 50 consecutive X-ray cases to compare with 50 radium cases, and whereas 82 per cent of the cases treated by radium therapy were cured, 100 per cent of those treated by X-ray therapy were cured, and have remained so from three to six years after.

An analysis of my 280 X-ray cases shows further that the risk of malignant disease occurring in an irradiated uterus is no greater than, if as great, as the risk of carcinoma occurring in it or in any other organ of the body in an untreated case. Furthermore the menopausal symptoms have been shown to be no more severe—indeed not as severe—in irradiated cases than in those of the normal climacteric.

The Advantages of X-ray Treatment.

The advantages of X-ray treatment over surgical are the same as those of radium over surgical, except that in a certain number of cases even a diagnostic dilatation and curetting is not necessary. Another advantage is that patients after X-ray treatment all report that they feel younger and better than they

TABLE IV.

Results of 280 cases treated by X-ray therapy. 1914–1934.

No. of cases	Cured	Not cured	Not traced	% not cured	Hysterectomy subsequently performed		Operations performed subsequently for disease of other organs	
					Non-malignant.	Malignant	Non-malignant.	Malignant
Ages 25 to 40— 59 Ages 41 to 58—221	261	10	8	3·5	10	4 (1 case carcinoma of cervix 15 years after, 1 case carcinoma of fundus 7 years after, 1 case carcinoma of fundus 3 years after, 1 case sarcoma of fibroid 5 years after)	5 1. Large ovarian cyst. 2. Ovarian cyst. 3. Cholecystectomy. 4. Cyst of breast. 5. Thyroidectomy and appendicectomy.	7 (Carcinoma of ovaries 7 years after, carcinoma of stomach 2 years after, carcinoma of breast 1 year after, carcinoma of breast 4 years after (very well now), carcinoma of breast 4 years after (very well now), malignant disease of the kidney 10 years after, malignancy of abdomen 5 years after)
Total 280	261	10	8	3·5	10	4	5	7

TABLE V.

Showing the results in 100 consecutive cases treated by irradiation.

Radium Therapy.			Intensive X-ray Therapy.		
No. of cases	Cured	Not traced	No. of cases	*Cured	Not traced
50 (1926–1934)	82%	3	50 (1929–1932)	100%	0

* The word "cured" in this context means—

(1) Relief of symptoms (pressure, menorrhagia).

(2) Amenorrhoea of one year or longer in patients under the age of 40 years, and complete in patients over 40 years of age.

(3) In the case of fibroids, a reduction of the tumour to at least one-third of its original size.

have felt for years; indeed, the number of grateful letters one receives is very striking.

Choice of Radium versus X-ray Therapy.

The extent to which X-ray therapy is used on the Continent is shown in the mass statistics collected by von Ammon for the years 1922 to 1927. He reports 6,967 cases treated with X-rays, 1,866 cases treated with radium, and 584 cases treated with X-rays and radium. This priority of treatment by X-rays is seen not only in Germany, where it could be explained as due to the scarcity of radium, but also in France and Sweden, countries richly supplied with radium.

A few authors, notably Kupferberg, Schaedel, Van de Velde, Weibel, Koblanck, Nogier, Cheron, Clark and Block, F. A. Cleland, Danforth, Edling and Keene, prefer radium treatment for fibromyomata.

Comparison of the Value of Radium and X-ray Therapy.

The advantages of X-ray therapy over radiotherapy are the following:

(1) With X-ray therapy the mortality is nil. Gauss collected 7,079 cases treated with seven deaths (0.098 per cent), but in the seven cases examined he was satisfied that they occurred in spite of the X-ray treatment, which was not the cause.

(2) There are not any resulting complications such as cystitis, pyometra, post-operative radionecrosis, with prolonged leucorrhoeal discharge, vaginitis, or dyspareunia so often seen after radium.

(3) The method is applicable to fibroids if interstitial and the size of a four months' pregnancy. In such cases the dose of radium has to be very large and is therefore sometimes followed by radionecrosis.

(4) The results are more certain, the percentage of cures being higher.

(5) There is not any fear of a stenosed cervix.

(6) It is safer if there is any likelihood of a latent adnexal inflammation. The trauma of dilatation and curetting in such cases may set up salpingitis or peritonitis.

The advantages of radiotherapy over X-ray therapy are the following:

(1) The cessation of haemorrhage is quicker. In a very anaemic patient this is important.

(2) If the patient is already bedridden, the blood-count as low as 2,000,000 reds, with a haemoglobin of 18 to 25 per cent, I give one or two blood transfusions, and directly the haemoglobin is higher apply the dose of radium necessary.

(3) If a diagnostic dilatation and curetting is imperative it is simpler to apply the radium at once.

(4) It is cheaper and simpler; X-ray therapy requires expensive apparatus, high voltage, and skilled administration; and regular and frequent calibration of the apparatus and tubes so that the accurately standardized dose is given.

Conclusions.

That deep X-ray therapy is the method of choice in all uncomplicated cases of climacteric haemorrhage due to metropathia haemorrhagica, fibrosis uteri, and small interstitial fibroids, in which menorrhagia is the main symptom and the degree of anaemia not so severe that the patient's life would be threatened if she were to have another severe period.

That radium therapy should be chosen in cases of climacteric haemorrhage due to the same causes, if the anaemia is severe enough to necessitate blood transfusion, and immediate cessation of haemorrhage if the patient's life is to be saved.

That surgical treatment is indicated in all cases of doubtful diagnosis, and if the fibroid tumour is larger than that of a four months' pregnancy; in all cases of subperitoneal and submucous fibroids and in cases complicated by neoplasms of ovaries or Fallopian tubes, or co-existing pregnancy; and that abdominal myomectomy be chosen in all young patients when possible in order not to interfere with the possibility of a future pregnancy.

Observation on the Aetiology of Abruptio Placentae and its Response to Vitamin E Therapy

BY

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PREMATURE separation of the normally implanted placenta has been described under a great variety of names. Accidental haemorrhage has been widely favoured. This term, however, connotes an association with trauma which, although it has been observed and dreaded by primitive peoples,[1] is seldom noted today; it would appear from our studies to be of very secondary importance. As first used by Rigby, accidental haemorrhage was meant merely for contrast with the unavoidable haemorrhage of placenta praevia. Concealed haemorrhage, another descriptive designation widely used, has a useful significance in emphasizing that there is not often a visible haemorrhage associated with such placental separation. This point has been well brought out recently by Goodall,[2] who in 750 placentae obtained from consecutive deliveries, found that 600 bore evidence of some haemorrhagic lesion, but in only 11 instances had there been vaginal bleeding during gestation. Rudolph Holmes[3] suggested ablatio placentae for the name of this condition, but that ignores the fact that such a separation of the placenta may be, from first to last, very partial, and certainly is usually incomplete at the time when clinical symptoms and signs first develop. Moreover the term does not convey any adequate picture of the common pathological events as they occur in the development of the lesion. This last objection could also be urged against the other names mentioned above with quite as much force. The author prefers the term abruptio placentae, suggested first by his inspiring preceptor, Prof. J. B. De Lee.[4] This name indicates something of the pathological picture and sequence of events, namely, a rupture of the vascular elements of the decidua basalis, a rupture of the placenta from its site, and a further rupture of blood into the uterine wall, amniotic sac or into the vagina.

Many cases of this pathological type are overlooked in both hospital and home practice, because placentae are not examined

routinely and carefully by competent obstetrical pathologists. This is especially true of the placental material in cases of abortion and miscarriage. Davis and McGee[5] pointed out that abruptio was much more common than had been believed, and gave a table in which various authors estimated its incidence in pregnancy at anything from 0.18 per cent (Kraul) to 1.06 per cent (Cragin, Goethals). The recent report of Baird[6] from Glasgow indicates an incidence there, in 10 years experience of 41,559 cases, of 2.8 per cent.

There are obvious difficulties in the way of an experimental approach to the problem of the aetiology of this lesion. Human experiment is obviously practically impossible. The placentae of the usual laboratory animals differ considerably in their architecture from that of man. Browne[7] attempted to produce premature separation of the placenta in rabbits by producing oxalate or uranium nephritis and then superimposing a bacillus pyocyaneus infection. Hofbauer[9] produced subplacental haemorrhagic lesions in guinea-pigs intoxicated with histamine. Datnow[9] by means of the use of selenium and cadmium salts produced haemorrhagic lesions in the placentae of pregnant rabbits.

Many workers have found that pregnant laboratory animals abort spontaneously on vitamin-defective diets. When they do so, whether the defect in the diet is with respect to vitamins B, C or E, the principal lesion appears to be a haemorrhagic separation of the placenta from the uterine wall. This has been amply demonstrated by the reports of Vogt,[10] Maxwell,[11] Evans,[12] Juhasz-Schaffer,[13] and Urner.[14] The same type of acute haemorrhagic subplacental lesion has been produced by means of the injection into the normal pregnant animal of oestrin or anterior pituitary preparations by Kelly,[15] D'Amour and Gustavson,[16] Teel,[17] Zondek,[18] and others.

Clinical Observations.

Our attention was directed to the problem of abruptio placentae in the course of a study of cases of miscarriage and abortion. Syphilis was found to be a negligible factor among pregnant women in this part of Canada. Indeed, there was not a single instance of a positive blood-Wassermann reaction in the cases of pregnancy of all types which we have studied in the last three years. We were impressed, however, with the frequent occurrence in our pregnant women of a certain definite group of symptoms and signs, which at any time might come to be associated with uterine haemorrhage and the interruption of preg-

nancy. The most frequent and significant sign was the gradual appearance of a restricted, palm-sized area of true uterine tenderness, accompanied by steady sacral backache. Occasionally uterine contractions, violent foetal movements and uterine haemorrhage of any grade of severity appeared as early or late sequelae. Or a gradual elevation of blood-pressure might ensue with oedema of the extremities, a rapid increase in weight, and even albuminuria—the usual evidences of the onset of toxaemia of pregnancy. In some instances our attention was first focused on the case because the foetus seemed unusually small, or because there was an excess of amniotic fluid. The uterine tenderness in severe cases usually spread to involve the whole uterus, but was always most intense at the site of its first appearance. On the other hand, all evidence of tenderness and associated symptoms might spontaneously disappear. When these symptoms reappeared, as they often did, the tender area was in the same location as before. In two instances, one a Caesarean section, and the other a manual removal of the placenta in a case of twins, we were able to prove that the placental site corresponded to the area of tenderness before the delivery. We do not know how many of these women would have gone on to show the classical evidences of toxaemia of pregnancy. Certainly many of them displayed such signs when the lesion was first discovered. The intensive therapy we instituted on the first appearance of signs of abruptio placentae may have prevented such further development in the treated cases. It is of interest in this regard that nearly three centuries ago Nicolaas Tulp, whom Rembrandt painted in *The Anatomy Lesson*, pointed out in his Monita Medica[19] that "in pregnant women, the sharp side-ache necessitates as much blood-letting as the case may demand".

We are well aware that the classical description of the lesion under discussion stresses generalized uterine pain and tenderness, nausea and emesis, systemic signs of haemorrhage, uterine evidences of haemorrhage, the development of a ligneous consistence of the uterus, shock, agonal foetal movements, and definite changes in blood-pressure. It is felt, however, that the cases so described are late and severe, and no more give a complete representation of the phenomena associated with abruptio, than pregnant women with polyneuritis and icterus, who have been vomiting violently for a long time, might be said to represent the classical picture of hyperemesis gravidarum.

When such cases as we have described went on to miscarriage or delivery before or at term, the placenta, which was often

unusually small, displayed one or more marginal lesions, which ranged from fresh clot through recently organized 'cream cheese' clot to white infarcts. These were seen on the maternal aspect of the placenta, although the infarcts as often as not extended through to its foetal aspect. When placentae were routinely inspected for these marginal lesions one was surprised to note their great frequency, a frequency comparable with that reported by Goodall. Patients who had been quite well throughout pregnancy might deliver a placenta which was as badly marred as the placenta expelled in a case of Couvelaire's apoplexy. On close inquiry these women usually could recall a period of toxaemia which had subsided with or without treatment, one or more haemorrhages of mild or severe degree during gestation, and a transient but definitely localized area of uterine tenderness, which, if it subsided and then recurred, always recurred in the same location.

We believe that this type of case represents premature and incomplete placental separation of varying degrees of severity. That there are mild and severe lesions of this sort has been very well brought out recently by Fitzgibbon[20] and by Rivett in the discussion of Fitzgibbon's paper.

Experimental Observations.

It occurred to us that much the same mechanisms responsible for the occurrence of haemorrhagic subplacental lesions in the laboratory animals might be responsible for similar placental separations in the human female. Accordingly we investigated a series of such clinical cases for any evidence of the imbalance between vitamin E and oestrogenic substance in the blood-serum, for which we have developed a simple laboratory test.[21, 22, 23] We studied the blood-sera of these patients for evidence of vitamin C deficiency as well, by a spectroscopic method based upon that given by Morton.[24] These studies on vitamin C are incomplete as yet, but we may say in passing that they do not indicate any vitamin C deficiency in human females who show the placental lesion under discussion. Moreover, we have seen cases of abruptio in women whose intake of vitamin C was abnormally large—as was, in fact, true of the most severe case in our whole series.

Our procedure in the testing of blood-serum samples has been described in detail elsewhere[21] and, therefore, need not be repeated here. All pregnant or recently delivered women were tested who showed the clinical or placental signs and symptoms

indicated previously, and later the serological results were correlated with the completed data on the case. Almost all these women were personally interviewed in order to obtain an accurate and careful history.

Our results are tabulated below. In the first year of our study of abortions and miscarriages we paid very scant attention to the abruptio group of cases. Moreover we were using a less sensitive testing substance than was developed later. Hence the results are tabulated separately from those of the later period. We excluded five cases from consideration, in which the testing had been done long after the placental detachment had been responsible for foetal *exitus in utero*, because our test for relative excess of oestrogenic substance in the blood is useless very soon after complete placental detachment has occurred.

Duration of experiment	No. of cases	Percentage showing an excess in the blood-serum of oestrogenic substance (in respect to the vitamin E—oestrogenic substance balance)[22]
January 1, 1934, to January 31, 1935	5 cases	80 per cent
February 1, 1935, to March 31, 1936...	60 cases	75 per cent
27 months in all ...	65 cases	75 per cent

It soon appeared that there was a close correlation between the development of this clinico-pathological syndrome and the occurrence in the blood-serum of these patients of a definite change. This change was a characteristic excess of oestrogenic substance in the blood-serum, which we have shown develops in conditions in which there is a bodily deficiency of vitamin E.[22] The correlation, indeed, between this serological change and the onset of signs and symptoms of abruptio was at least as close as that which existed between the same serological phenomenon and the onset of abortion or miscarriage. It was natural, therefore, to attempt therapy in these cases with vitamin E, and we did so, using a potent preparation with which we were thoroughly acquainted (viteol, supplied by Canada Pharmacal Company, London, Canada). We have been greatly pleased with the success of such therapy, although, of course, it can necessarily be of little use in those cases first seen when complete detachment of

the placenta has already occurred, associated with great haemorrhage and shock. We feel that a closer search for uterine tenderness during pregnancy and a test made on the blood-serum early in pregnancy, or on the appearance of such tenderness, for the hormone-vitamin imbalance that has been described would, at least to a large extent, obviate the development of such severe cases. We hope that further study may clarify this point.

In any event, we can state that an adequate massive dose of a potent preparation of vitamin E has completely abolished in approximately 20 hours the circumscribed area of uterine tenderness seen in almost all of these cases. The accompanying sacral backache and uterine cramps have subsided quite as rapidly. Uterine haemorrhage, when present, has stopped promptly. The indescribable subjective symptoms, related by a physician's wife who developed a Couvelaire apoplexy of the uterus as "like a cold coming on", have disappeared within the first day of treatment. When such therapy has been stopped, uterine tenderness and bleeding have often reappeared, only to disappear with characteristic rapidity on further vitamin E therapy.

Discussion.

The best therapeutic results, as would be anticipated, have been obtained in patients who showed little or no evidence of an associated toxaemia. We do not feel capable at present of discussing the relation of toxaemia to abruptio placentae and its vitamin therapy, although fascinating problems present themselves here. All that we can say at present is that in our patients in whom the toxaemia was detected early, at the first rise of blood-pressure, at the first rapid gain of weight or appearance of oedema, or in whom by abdominal palpation the baby seemed strikingly small for the duration of gestation, wheat-germ oil therapy was promptly associated with a return of the blood-pressure to normal levels at which it was maintained. Moreover, any unusual rate of weight increase was decreased, as well as any obvious oedema—and all this without the imposition of salt restriction in the diet, rest in bed and other such measures. Some of these small foetûs seemed to gain in size in an amazing way. We are well aware of the fallacious character of clinical estimations of foetal size, however, and are now supplementing these observations by Roentgenological studies. In those cases in which evidences of toxaemia had been noted for a period of weeks or months before vitamin E therapy had been begun, and evidence of renal involvement such as albuminuria or defective concentra-

tion of urine had already appeared, the wheat-germ oil produced only a transient but definite fall of systolic pressure. Such cases, in our limited experience, have not progressed to true eclampsia, however, and with adequate vitamin E therapy labour could be safely induced when gestation was more advanced. The placentae adhered sufficiently well to enable living children to be born.

As this is intended for a preliminary report, we cannot dwell on the relation of pregnancy toxaemia to the subject under discussion. Suffice it to say that, in a small group of true convulsive eclamptics, we have never yet found evidences in the blood-serum of the imbalance between vitamin E and oestrogenic substance which produces a relative excess of the latter. Indeed, the Smiths[25] have shown that there is a high content of chorionic gonadotropic hormone and a low oestrin content in both the blood and placentae of eclamptics. On the other hand, Heim[26] has reported that in toxic cases of premature separation of the placenta there may be as large an excretion of oestrin in the urine as in cases of hydatid mole and chorion-epithelioma. He found that in cases of eclampsia and eclampsism, on the contrary, the prolan excretion, as well as oestrin excretion, rose to very high levels. There may, therefore, be some justification for looking forward to a better classification of the toxaemias of late pregnancy, perhaps into a group in which convulsions impend and a group in which premature placental detachment impends. The former may be characterized by high blood-contents of chorionic gonadotropic hormone and the latter by high levels of blood oestrin. Such a division of the toxaemias was partially foreshadowed years ago by Holmes, who insisted on the rarity of abruptio in eclamptics.

An interesting development of this study is in the differential diagnosis between placenta praevia and abruptio placentae. Vaginal examinations intended for this purpose are sometimes dubious and always dangerous. Roentgenological methods leave much to be desired, as appears from some of the conflicting reports[2, 7, 28] in the literature. We have had very few cases of placenta praevia, but have never yet found in any of them the relative excess of oestrogenic substance in the blood which our test will indicate. The clinical details and corroborative serological test we have described may be of some assistance in dealing with a problem in differential diagnosis which is often puzzling.

In conclusion, we believe that a very important factor in the aetiology of abruptio placentae is the appearance in the blood-serum of an imbalance between vitamin E and an oestrogenic

substance. The effect of such an imbalance is to produce a relative excess of oestrogenic substance. This develops weeks and even months before the symptoms and signs of abruptio show themselves. Correction of this disturbance by means of the administration of a potent vitamin E preparation is of great prophylactic and therapeutic value. The pessimistic view expressed recently by Baird that "antenatal care can do little in the prevention of accidental haemorrhage" appears, therefore, to be gloomy. It is even conceivable that if all pregnant patients were treated adequately with a potent vitamin E from the beginning of pregnancy, the incidence of abruptio placentae would be reduced to very small dimensions. Moreover, we feel that a very interesting approach to the problem of the toxaemias of pregnancy, as well as to the broader problem of nephritis, is disclosed by this work.

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MATERNITY HOSPITAL REPORTS

As everybody knows, figures can be manipulated to prove anything, even the impossible. Nevertheless, an honest analysis of the results obtained in a large series of cases is of considerable value. Some complications are of such frequent occurrence that a single observer may, from his own experience, form accurate conclusions, but for the study of the rarer abnormalities it is essential to supplement a limited personal knowledge by combining the published results of several workers. To facilitate this object, a special scheme for the Unification of Maternity Hospital Reports was drawn up some years ago, and the majority of institutions agreed to adopt it. For a time they did so, but of late there has been a tendency for the compilators to depart from it. As a rule they have not improved upon the original, and even if they had, they have defeated the primary object. Hospitals in which a large number of abnormal cases is dealt with are inclined to frame their reports in such a way as to emphasize this fact, whereas others in which few complications are encountered are tempted to modify the arrangement of their reports to illustrate some point which they believe to be of interest. But it matters nothing at all that one institution treats five times as many cases of contracted pelvis as another, that a third admits patients from a restricted area, while in still another practically all the patients are "booked". What does matter is that the experience of all be made available for everyone by uniformity of reporting.

We understand that the British College of Obstetricians and Gynaecologists is engaged in drawing up a case-sheet on which to report cases treated at Maternity Hospitals and Maternity Departments of General Hospitals. We sincerely hope that this case-sheet will soon be forthcoming, and that the Chiefs of Departments will personally insist on their Registrars using such a case-sheet, and not, as heretofore, being merely satisfied with their own approval of such a case-sheet.

University College Hospital, London

REPORT FOR THE YEAR 1935.

THIS report has been prepared with great care, and the facts are presented in great detail. But the Committee's scheme has not been followed and the value of the report is correspondingly reduced. For some reason not stated the Registrar has introduced a group of "referred" patients, in addition to the agreed classification into "booked" and "emergency" cases. There is no justification for this increased complexity. The total number of patients is small, and very few abnormalities are encountered among them.

This passion for subdivision is evidenced in other directions. Four degrees of placenta praevia are described, although there are only 14 patients

of this type. If the new classification were good we should welcome it, but in our opinion it is not. Again, there are 128 subdivisions in the table giving a few facts regarding 71 cases of abortion, and no fewer than 63 of the pigeon-holes are blank. The methods of anaesthesia and analgesia employed in the different types of case are set out in a table of 138 subdivisions which is disagreeably reminiscent of permutations and combinations. It conveys nothing to the reader and apparently almost as little to those who laboriously compiled it, for the only comment which they add is the simple remark that "in no case did the anaesthetic appear to have any deleterious effect on the mother or child."

In the gynaecological part of the report the reader is again given much meaningless information, when a less detailed statement of the facts would have served the purpose. We are not told, for instance, that 59 cases of prolapse were treated during the year: we have to add up 59 separate items for ourselves. Yet serial numbers which we cannot use are supplied profusely as follows:

" 2. Prolapse.

"Anterior colporrhaphy, posterior colpoperineorrhaphy, and amputation of cervix, Z17, Z54, Z91, Z102, Z116," and so on.

It is a pity that so much careful work should be wasted in this way, and the reviewer regrets the necessity of devoting so much space to criticism of a report which has been prepared with such diligence. But minute tabulation, unaccompanied by a clear summary of the main facts, merely leads to confusion. We are of the opinion that the majority of readers will refuse to take the trouble of resolving the extended tables to a simpler form and will put this report aside unstudied.

Maternity Department of Guy's Hospital

REPORT FOR THE YEAR 1935.

"IN this report the classification has followed the lines adopted in the reports for previous years, and the reasons for departing from the classification recommended by the Sub-Committee for the Unification of Reports of Maternity Hospitals remains the same. . . . It has been found impossible to give any useful classification on the basis of 'booked' and 'emergency' cases, since practically all cases belong to the first class." So the Registrar explains in the introduction. The argument does not appear to us to be very convincing, for, so far as we can see, the matter would not be impossible. All that would result from following the recommended scheme is that one group would be large and the other small. But the data could be used in conjunction with the results from other institutions, whereas the figures in their present form are of no use to anyone.

The report as such has been reasonably and accurately compiled, but the abnormalities are so few in number that there is no need to discuss the findings. It seems strange, however, in view of the comparatively simple nature of the cases, that fully 9 per cent of them should have had a post-

partum haemorrhage. Incidentally, there is some dubiety as to the actual number, which is given as 112 on page 6, and as 101 on page 19. From the detailed table we find the number to be 115, or at least it is so if we correct the faulty addition in the second column.

Liverpool Maternity Hospital

REPORT FOR THE YEAR 1935.

OF the 4,080 patients attended by this hospital, 2,416 were treated in the wards, and with these patients the report deals in detail. The proportion of abnormal cases is high, and the reader will find the data of much interest. Particularly satisfactory are the tables on cardiac disease, albuminuria, antepartum haemorrhage, and induction of labour.

Forty-one cases of heart disease were treated, and although many of them were obviously of a severe type, only one ended fatally. Caesarean section was chosen as the method of delivery in 16 of them, hysterectomy was performed on two occasions, while abortion was induced in one case by means of X-rays. The results in the 90 cases of albuminuria are equally good. Only one mother died, and it would have been surprising had she recovered, since she suffered from a severe degree of nephritis and a super-added pyelonephritis. There were only three cases of pernicious vomiting, but one of them is most interesting. Her history and treatment are reported in full, the unusual feature being the successful employment of decapsulation of the kidney in overcoming an almost complete anuria. Another series of cases reflecting great credit upon staff is the group of 13 patients in whom the placenta was removed manually. There were no maternal deaths, and only one patient developed pyrexia. It is instructive to note how long the placenta was allowed to remain in the uterus before extraction. In one instance the interval was 54 hours.

A special section of the report deals with infant mortality, clinical causes of death, post-mortem findings, congenital deformities, birth injuries, diseases of the newborn, infant feeding, prematurity, and abnormally large infants. This portion is very good indeed. It does not lend itself to summary, but it will repay a most careful study.

In view of the general excellence of the report it seems almost ungracious to draw attention to some minor slips which mar its perfection. There are, however, a number of arithmetical errors, and inattentive proof-reading has allowed several mistakes in the spelling of technical words to pass uncorrected.

The Princess Mary Maternity Hospital, Newcastle

REPORT FOR THE YEAR 1935.

DURING the year under review approximately 2,500 patients were treated in this hospital. Over 1,000 cases were admitted as emergencies, and in many the complications were of a severe type and of extreme degree. This is evidenced by the summarized case-histories and by the foetal death-rate

in abnormalities such as accidental and unavoidable haemorrhage. The standard of obstetrics in the surrounding district would not appear to be very high, as no fewer than 38 cases were sent in to hospital after failure to deliver with the forceps. In this group the over-all maternal mortality was 22 per cent, and the foetal mortality over 50 per cent. The hospital staff in such circumstances must undoubtedly work at high pressure, and this may explain the incompleteness of the records which is apparent in certain sections of the report. For instance, the blood-pressure is not recorded in several of the albuminuric patients, and the amount of albumin is indicated as +, ++, +++, solid, or trace, and never as so many parts on the Esbach scale. Forty-three cases of eclampsia occurred during the year, and of these three were "booked" cases. In the foreword it is stated that "two of them died, and from their histories it is evident that antenatal care could not have saved them." Unless the history given omits one very important item, then this assertion cannot be held as proved. One of the two patients attended the antenatal clinic five days before admission. The urine did not contain any abnormal constituent, and the patient did not have any toxic symptoms. She was perfectly well until nine hours before admission . . . etc. . . . So far so good, *but it is not stated in the report that her blood-pressure was taken at the time of her visit.*

There is nothing of special note in the rest of the report, except that it is somewhat curious to find vaginal sepsis, pelvic cellulitis, perineal sepsis, uterine sepsis, pelvic abscess, salpingitis, phlegmasia alba dolens, mastitis, and breast abscess, included under the heading "non-morbid conditions". In calculating the percentages of the foetal deaths the Registrar frequently omits to make allowance for the fact that some of the patients in a given series are not delivered, while others have twins. Apart from this oversight the report is well drawn up.

County Borough of Croydon

REPORT OF THE COUNCIL'S OBSTETRIC SERVICE FOR 1935.

"The obstetric scheme in Croydon is perhaps the most complete of any of the schemes conducted by local authorities. It aims at the ideal of complete antenatal, natal, and post-natal medical supervision under the same whole-time medical officer. The antenatal clinics, Mayday Hospital, and St. Mary's Maternity Hospital are all links in the chain, working with one another under the clinical guidance of the specialist Assistant Medical Officer of Health for Obstetrics." Details are given in the appendices of the organization of the clinics, of the management of the two hospitals, and of the different methods of staffing them. These notes should be of much interest to all who have to organize a similar service.

Apparently the arrangement works well in practice, for the results obtained are very good. These results are fully set out according to the scheme for the Unification of Maternity Hospital Reports, and those who believe that the special conditions prevailing in their particular hospital

preclude the use of this unified plan, should reconsider their attitude when they find that the scheme can be adopted with perfect satisfaction to embrace the work carried on by the Croydon service.

The report itself is carefully compiled, and the completeness of the tables shows that the record-keeping in both the antenatal clinics and in the hospitals is unusually efficient. A special set of tables has been devised for the septic cases. These are excellently conceived and might well be copied by other registrars. Curiously enough, although this report is issued by a Public Health Authority, the standard of puerperal pyrexia employed is not that of the Ministry of Health. And here we may remark that in the five reports reviewed above four different standards of morbidity have been used.

John Hewitt.

INTERNATIONAL CONGRESS FOR OBSTETRICS AND GYNAECOLOGY

(AMSTERDAM, MAY 4—8, 1938)

President . . Prof. Dr. A. H. M. J. VAN ROOY, Amsterdam

PRELIMINARY NOTICE

THE Committee of the International Congress for Obstetrics and Gynaecology in May 1938, at Amsterdam, has fixed as principal subjects for discussion at the Congress the following:

(*a*) *Eclampsia—three reporters:*

1. Pathogeny.
2. Treatment.
3. Eclampsia, from a geographical point of view.

(*b*) *Thrombosis and Embolism—three reporters:*

1. Diagnosis and symptomatology.
2. Aetiology.
3. Prevention and treatment.

(*c*) *The Theory of the Hormones—three reporters:*

1. A historical review of the question of the hormones in so far as it is of significance to gynaecology.
2. Three lectures concerning the latest research work and their own work, and what can be expected of this method of treatment in the future.

The Preparatory Committee aims at inviting scientific workers from different countries as reporters.

Professor Daniel Dougal, *M.C.*, M.D., Ch.B., F.C.O.G., has been invited to report on "The Aetiology of the Thrombosis and Embolism".

BOOK REVIEWS.

"Radiotherapie Gynecologique—Curie et Roentgentherapie." By R. MATHEY-CORNAT, Radiologist des Hopitaux. Medecin de la Fondation Bergonie (Centre anticancereux de Bordeaux et du Sud-Ouest. Chef du Service central d'Electroradiologie des Hopitaux du Groupe Pellegrin-Le Tondu. (Masson et cie, Paris; 1936). 369 pp. 60 fr.

THIS book, by one of the members of the Anti-Cancer Centre at Bordeaux, is written almost exclusively from the clinical standpoint and describes the radiological methods of treatment employed in gynaecology; it is, however, not restricted to this subject for section No. 7 (26 pages) is devoted to malignant and non-malignant conditions of the breast and their treatment.

Some idea of the scope of the book may be gathered from a brief recital of the contents of the remaining sections. The first is devoted to a short account of the action of the rays upon the uterus and uterine tumours, then follows one on the technique of the appliances used in treatment with some account of dosimeters and of the methods of calculating what are known as "depth doses". Non-malignant affections, including disorders of menstruation, inflammatory and tuberculous conditions, their treatment and results, together with radiological methods of sterilization, are the subject matter of the next four sections of the book. This is followed by the biggest section in the book, devoted to the diagnosis and treatment of malignant conditions of the genital system; the section is divided into four chapters dealing respectively with affections of the vulva, vagina, uterus and ovary.

The book should prove, in its clinical completeness, of value to gynaecologists and to many besides. The author may be induced in a later edition to supplement the rather slender statistical information to be found in these pages; this should now be possible, as many reliable clinics provide statistical data over periods of more than five years.

The book has a very useful bibliographical index containing complete references to no less than 563 published papers.

S.R.

"A Centenary History of the Manchester Medical Society." By E. M. BROCKBANK, M.B.E., M.D., F.R.C.P. (Sherratt & Hughes, Manchester; 1934.)

THIS is a short, readable account of the Manchester Medical Society written by an author well versed in local history. The main details of its formation, growth, and constitution are given briefly, and justifiable pride is shown in the description of its library, which contains many rare editions of medical works. In the latter part of the book biographies are given of four of the most famous of the Society's members.

The story of a Medical Society provides a recapitulation of the development of medicine, and in this history of the Mancheshter Society one is

reminded of the controversies which have raged during the last one hundred years; fights which were repeated in individual details in all our large cities.

Obstetricians have apparently played their part well in the Society, both in controversy, as is their custom, and in constructive effort. The first President of the Society was Dr. Hull, a well-known North of England obstetrician, to whom we owe the phrase *phlegmasia alba dolens*; and Dr. Cullingworth, who migrated later to St. Thomas's Hospital, was an Honorary Librarian.

R.K.B.

Review of Current Literature.

Director: FREDERICK ROQUES, M.A., M.D., M.Chir. (Cantab), F.R.C.S., M.C.O.G.

THIS Review contains the lists of contents and abstracts of the more important articles from the following journals with which the "Journal of Obstetrics and Gynæcology of the British Empire" exchanges :—

British.—The Lancet; British Medical Journal.

Canadian.—The Canadian Medical Association Journal; Bulletin Médical de Quebec.

Australian.—Medical Journal of Australia; The Australian and New Zealand Journal of Surgery.

Indian.—The Calcutta Medical Journal.

American.—American Journal of Obstetrics and Gynecology; The Journal of the American Medical Association; Surgery, Gynecology and Obstetrics; American Journal of Diseases of Children.

French.—La Gynécologie; Gynécologie et Obstétrique; Bulletin de la Société d'Obstétrique et de Gynécologie de Paris.

Belgian.—Bruxelles Médical.

Italian.—Annali di Obstetrica e Ginecologia; Archivo di Obstetrica e Ginecologia; Revista Italiana di Ginecologia, Bologna.

German.—Archiv für Gynäkologie; Zeitschrift für Geburtshülfe und Gynäkologie; Zentralblatt für Gynäkologie; Monatsschrift für Geburtshülfe und Gynäkologie; Münchener Medizinsche Wochenschrift; Monatsschrift für Krebsbekampfung.

Scandinavian.—Acta Obstetrica Scandinavica.

South American.—Boletin de la Sociedad Obstetricia y Ginecologia de Buenos Ayres.

Japanese.—Japanese Journal of Obstetrics and Gynæcology.

The Review of Current Literature thus keeps the readers of the Journal in touch with current literature throughout the world. At the end of the year an Index of all the subjects contained in the articles of the above journals is printed. Arrangements are also made to include abstracts of important articles on border-line subjects, such as Physiology, Biology and Biochemistry.

LIST OF ABSTRACTORS.

London: J. BEATTIE, F.R.C.S.; A. C. BELL, F.R.C.S.; R. K. BOWES, F.R.C.S.; J. LYLE CAMERON, F.R.C.S.; A. H. CHENARD, M.B.; R. L. DODDS, F.R.C.S.; B. GILBERT, Esq., F.R.C.S.; R. C. LIGHTWOOD, M.D.; J. A. MOORE, M.B.; C. D. READ, F.R.C.S. (Edin.); F. ROQUES, F.R.C.S.; R. WINTERTON, F.R.C.S.

Huddersfield: W. E. CROWTHER, M.B.

Leeds: R. H. B. ADAMSON, M.D., AND B. JEAFFRESON, F.R.C.S.

Liverpool: M. DATNOW, M.D.; P. MALPAS, F.R.C.S.; T. N. A. JEFFCOATE, F.R.C.S.

Manchester: R. NEWTON, M.D.

Glasgow: JANE H. FILSHILL; R. SHARMAN, M.D.

The Journal of Pathology and Bacteriology.

Vol. xliii, 1936.

*Histological changes in the sex organs of spayed rats induced by testosterone and oestrone. V. Korenchevsky and M. Dennison.

HISTOLOGICAL CHANGES IN THE SEX ORGANS OF SPAYED RATS INDUCED BY TESTOSTERONE AND OESTRONE.

The uterus, vagina and preputial glands of 60 rats were examined histologically after giving testosterone and oestrone. The appearances were compared with those found in 26 normal rats and 56 spayed rats into which oestrin had been injected. The effects of oestrone on the vagina and uterus were different from those of oestrin in normal rats. Testosterone without oestrone brought about a partial return to normal in the uterus and vagina. Testosterone with oestrone produced changes similar to the changes seen in the vagina during pregnancy and in the pro-oestrous uterus. Androsterone-diol produced similar effects to those of testosterone, but these effects did not follow the injection of androsterone.

J. Moore.

Johns Hopkins Hospital Bulletin.

Vol. xxxix, No. 2, 1936.

*Mesenteric Tumour associated with Pregnancy. E. Henriksen.

Vol. xxxix, No. 4.

*Samonella suipestifer infection in myomata of the uterus. L. Gray.

MESENTERIC TUMOUR ASSOCIATED WITH PREGNANCY.

A case of a mesenteric tumour resembling a benign myoma is described in association with a pregnancy of 10 weeks.

SAMONELLA SUIPESTIFER INFECTION OF UTERINE MYOMATA.

A case of suipestifer septicaemia with multiple abscesses in uterine myomata is described. The fibroids had greenish-yellow necrotic centres from which samonella suipestifer was isolated. The abscess in each fibroid was probably metastatic from the general infection. Other cases of samonella infection of the female organs are reviewed.

J. Moore.

The Journal of Physiology.

Vol. cxxxviii, No. 1, 1936

*The action of progesterone on the uterus of the rabbit and its antagonism by oestrone. J. M. Robson.

THE ACTION OF PROGESTERONE ON THE UTERUS OF THE RABBIT AND ITS ANTAGONISM BY OESTRONE.

The ovaries were removed from mature rabbits and the animals were then injected with oestrone for seven or eight days. They were then divided into three groups:

1. Those given progesterone.
2. Those given progesterone and oesterone.
3. Controls, which were not injected.

After four days observations were made of the histological condition of the uterine endometrium, of the uterine muscle to extracts of the posterior lobe of the pituitary gland, and of the spontaneous rhythmic activity of the uterine muscle. It was found that a dose of 0.75 milligram of progsterone usually produced a degree of progestational proliferation equivalent to that observed in pseudo-pregnancy. The effect of progesterone on the endometrium could be completely inhibited by the simultaneous injection of one seventy-fifth part of its weight of oestrone. Progesterone produced desensitization of the reaction of the uterine muscle to oxytocin. When oestrone was simultaneously administered the desensitization *in vitro* may be somewhat decreased, but full desensitization of the muscle *in situ* was consistently obtained. Vasopressin may produce inhibition of the uterine muscle *in situ*. This inhibition was always obtained in animals treated with oestrone.

J. Moore.

The Canadian Medical Association Journal.

Vol. xxxv, No. 3, September 1936.

*The relation of maternal anaemia to foetal polycythaemia. George J. Strean and Rudolf Gottleib.

*A further report on obstetric analgesia and amnesia. Leighton C. Conn and John Ross Vant.

*The value of blood-sugar in the treatment of damage to the birth canal. C. V. Ward.

*The radiological treatment of cancer: methods and results. (1), The biological conception of dosage in radiotherapy. G. E. Richards.

Vol. xxxv, No. 4, October 1936.

*The radiological treatment of cancer: methods and results. (2), Carcinoma cervicis uteri from 1928 to 1935. G. E. Richards and W. G. Cosbie.

*Pregnancy complicated by rheumatic heart disease. D. N. Henderson.

*Congenital absence of the cervix uteri complicating pregnancy. D. W. Davis and J. F. Haszard.

THE RELATION OF MATERNAL ANAEMIA TO FOETAL POLYCYTHAEMIA.

Polycythaemia is a well-established affection of the newborn, and is believed to be a compensatory reaction to intra-uterine anoxaemia resulting from a mixture of arterial and venous blood and from the inadequacy of the placenta as a respiratory organ.

The degrees of polycythaemia may vary markedly and seem to be increased by any factor which increases anoxaemia.

Maternal anaemia, a common occurrence during pregnancy, is believed to be a cause. Seventy-five consecutive non-selected cases were studied and the maternal blood was compared with the foetal blood obtained from the umbilical vein immediately before delivery, and it was found that all cases of maternal anaemia were associated with foetal polycythaemia. In

six of the cases of polycythaemia the maternal blood-picture was normal. A cause was believed to be pathological changes in the placenta.

As foetal polycythaemia is frequently followed by icterus neonatorum, which again may be associated with haemorrhage in the newborn and possibly with intracranial extravasation of blood, it is important to recognize all factors which have an aetological bearing on the blood-picture of the newborn.

As a result of these investigations the authors advocate examination of the maternal blood in all cases, and extensive treatment with iron when any degree of anaemia is present.

A short bibliography is appended.

A Further Report on Obstetric Analgesia and Amnesia.

The authors make a further report on 396 cases anaesthetized by nembutal given by the mouth and paraldehyde given by the rectum. In a few cases the dose of paraldehyde was repeated. Anaesthesia by nitrous oxide was added to this during the actual delivery of the child.

Satisfactory amnesia was obtained in 92 per cent of the cases. Pain was not relieved in only one per cent of the primiparae and four per cent of the multiparae.

Labour did not appear to be prolonged, nor in any case was spasm of the cervix or tonic contraction of the uterus encountered. The risk of injury to the foetal head did not appear to be increased, and the mothers made a good subsequent recovery. There appeared to be no untoward results either to the mother or the child which could be definitely attributed to the analgesic employed.

The Value of Blood-sugar in the Treatment of Damage to the Birth Canal.

Assuming the assurance that disturbances of carbohydrate metabolism were associated with delayed healing of wounds, it was presumed that incomplete healing of injuries and lacerations of the birth canal was due to an inability on the part of the patient properly to utilize sugar. The blood-sugar was found to be excessive in 110 cases, 26 of which had, in addition, glycosuria and were proven to be diabetics.

When diabetic treatment was instituted it was noted that all recent lacerations and operation wounds healed more readily than in the cases not so treated. This investigation appeared to show that there was a high incidence of disturbance of the carbohydrate metabolism in patients who applied for hospital treatment and that excellent results followed when the cases were treated with diet and insulin.

The Radiological Treatment of Cancer: Methods and Results. (1), The Biological Conception of Dosage in Radiotherapy.

A detailed report of results is not given, but the authors appear to be of the opinion that conclusions based upon statistics to establish figures are extremely risky.

It appears, however, that the immediate action of radiotherapy upon local lesions and pelvic masses has been extremely good.

THE RADIOLOGICAL TREATMENT OF CANCER: METHODS AND RESULTS. (2), CARCINOMA CERVICIS UTERI FROM 1928 TO 1935.

During this period 227 patients in the public wards were treated with radium supplemented by high voltage X-rays. Not any of these patients had previously received treatment such as subtotal hysterectomy. The number is not considered sufficient to permit an estimate of results to be made.

Out of this total number of patients 123 are still living. Three after six years, five after five years, 13 after four years, eight after three years, and 22 after two years. Of the 104 dead, 99 died of cancer. Of the living patients 89 are at present free from symptoms.

A second group of 34 patients was treated with radium, the dosage being 8,400 milligram-hours. A filter equal to 1.5 millimetres of platinum was used inside the uterus and one equal to 2.5 millimetres in the vaginal portion of the applicator. Great care was taken in placing the radium and avoiding trauma of the tissues. Thirty-two of these patients are living, 30 being free from symptoms: one after six years, two after five years, four after four years, one after three years, seven after two years, and 11 after one year. All of these were very early cases.

In another group of a later stage of the disease 82 patients were treated, of which 55 are living and 25 are dead from cancer. One is living after six years, two after five years, six after four years, six after three years, 10 after two years, and 12 after one year.

Another group of 68 cases of a more advanced stage was studied. Before high voltage X-ray therapy was used the deaths were usually more than 50 per cent in the third group. It was always more difficult to treat these patients owing to the mass of growth and secondary infection. Treatment was started in these cases with a very thorough and protracted course of high voltage X-rays. Each treatment lasted from 40 to 60 minutes, two such treatments being given per diem, over a period of four to six weeks. Radium treatment was instituted after the completion of a series of exposures to X-rays. In this group there were 69 cases, of which 29 were living and 39 dead at the end of the period. Of these one was alive after six years, one after five years, three after four years, one after three years, and four after two years.

In a further group of very advanced cases cure was not expected, but it was hoped to prolong life and relieve pain. There were 42 cases in this advanced stage; 35 were dead of cancer and seven were living at the end of the period. One patient was living after two years, one after one year, and five patients after less than one year, all under treatment.

In all advanced cases it was deemed preferable to institute high voltage X-ray treatment first, to be followed by the application of radium when its use was indicated.

PREGNANCY COMPLICATED BY RHEUMATIC HEART DISEASE.

Cardiac disease complicating pregnancy is a grave condition for both mother and child. The mortality among the mothers appears to be between 8.4 and 2.3 per cent. One thousand women die annually in the United States of America as a result of cardiac disease associated with pregnancy.

Hamilton and Kellog report that 25 per cent of the maternal deaths under

their observation were due to cardiac disease, and Schuman regards it as the second highest cause of maternal death.

The authors report on 35 patients suffering from rheumatic cardiac disease complicating pregnancy, and are of the opinion that such cases require careful prenatal investigation by both an obstetrician and a cardiologist, their special aim being to anticipate and prevent cardiac failure. They reach the conclusion that, when cardiac failure does not occur during pregnancy, it is highly improbable that it will develop as a result of normal labour.

Conservative methods of delivery are recommended, and Caesarean section is advised only in a limited number of exceptional cases. Repeated pregnancies are regarded as unfavourable, as there seem to be fairly clear indications that they tend to shorten the life of the patient and add to the risks of cardiac failure.

Termination of pregnancy is considered to be justified in many cases owing to cardiac failure.

A full bibliography is appended.

CONGENITAL ABSENCE OF THE CERVIX UTERI COMPLICATING PREGNANCY.

The case of a primiparae, aged 26 years, is reported. On examination she was found to have a short vagina and complete absence of the cervix uteri, the external os being very small.

The patient was given a trial labour. After 10 hours of very strong pains the cervix, although pushed down to the perineum, showed no signs of dilatation. Classical Caesarean section was performed, it being believed that in the absence of the cervix the lower segment operation could not be undertaken.

The progress of the case was satisfactory in every way, sufficient drainage of lochia occuring through the small os.

J. Lyle Cameron.

Medical Journal of Australia.

Vol. i, No. 21, May 23rd, 1936.

*Sterilization of the unfit. Paul G. Dane.

Vol. i, No. 23, June 6th, 1936.

Obstetrical obstacles. H. Stanley Waters.

*An evolutionary factor in parturition. The law of the split pelvis. C. D. Gillies.

Vol. i, No. 25, June 20th, 1936.

The law of the split pelvis. (Correspondence.) F. Wood Jones.

Vol. ii, No. 2, July 11th, 1936.

Fallopian tube and ovary in an inguinal hernia of an infant. E. R. Roseby.

Vol. ii, No. 5, August 1st, 1936.

*Frequency of micturition in the female. John Close.

Vol. ii, No. 8, August 22nd, 1936.

Avenues of progress in maternal welfare. Marshall Allan.

Vol. ii, No. 10, September 5th, 1936.

*The early diagnosis and treatment of intracranial injuries. Roland A. Nathan.

STERILIZATION OF THE UNFIT.

The author includes among the unfit all those who are unable to adapt themselves economically to the stress of the times. The lower limits of the group are obvious, but the upper are difficult to define. One per cent of the population in England is mentally unfit to earn a living, and between 3 and 15 per cent of delinquents are defective.

It is said that mental defectives are abnormally fertile, but in fact the grossly mental defective is not capable of breeding, and it is only those who are nearly normal who breed to any extent.

The majority of this subnormal group lives in the slums under conditions which bring about mental and physical deterioration. The author states that heredity does play a part, but the mental defect may come from a distant ancestor. He finds that mental deficiency is inherited in 50 per cent of cases.

It would take many thousands of years to eliminate mental deficiency by sterilization of the unfit. For every one mentally unfit person there are 10 carriers, and these would also require sterilization.

AN EVOLUTIONARY FACTOR IN PARTURITION. THE LAW OF THE SPLIT PELVIS.

The author describes the split pelvis as it occurs in the predentate dinosaurs, birds, and sporadically in certain orders of the mammalia, in response to the demands of parturition. The underlying evolutionary principle is the "law of the split pelvis", which states that when disproportion occurs between the products of conception and the pelvic brim, separation of the ventral symphysis occurs in those types which survive.

FREQUENCY OF MICTURITION IN THE FEMALE.

The author gives the anatomy of the urethra and supports of the bladder. Frequency of micturition results from acute and chronic urethritis. In chronic urethritis the urethroscopic findings are a polypoid condition of the internal meatus and bulbous oedema of the trigone, or a granular condition of the urethral mucosa, or no abnormal signs at all. Smears should be taken.

Cervical infections are treated. The urethra is dilated with a Kollman's dilator, and 0.5 per cent to 5.0 per cent silver nitrate solution instilled. Inflammation of Skene's tubules is common and is treated by destruction of the ducts, either by silver nitrate, or by slitting them open.

Infection, calculus formation and fibrosis occur in the so-called female prostate. Treatment is by Kollman's dilator.

Carcunculae are, in the opinion of the author, polypi at the mouths of the infected Skene's ducts. He treats them by dissecting out the lower half of the urethra, caruncle and glands, and removing them.

Trigonitis pseudo-membranosa, or exfoliative trigonitis, is due to pelvic congestion, usually of uterine origin. Cystocele is only the cause of frequency when there is residual urine and basal cystitis.

Stress incontinence can be cured by Bonney's operation, but the author disagrees with Bonney's reasonings.

Frequency due to neurosis occurs during the day only. Ephedrine, gr. ½, is beneficial in these cases. For cases which do not react to this treatment spinal anaesthesia of the sacral area has been advocated.

EARLY DIAGNOSIS AND TREATMENT OF INTRACRANIAL INJURIES OF THE NEWBORN.

Nearly 50 per cent of neonatal deaths are due to intracranial injuries. Many children who have small tentorial tears survive. The children are born in white asphyxia. Respirations are slow and irregular. There may be convulsions, rigidity of the neck, and unequal pupils. The sucking reflex is often absent. The child may be lethargic, or restless and whining.

In supra-tentorial haemorrhages the child is restless, and there is a bulging of the anterior fontelle. Cyanosis occurs later. In infra-tentorial haemorrhages the reverse is true, and the neck is rigid.

Lumbar puncture is of diagnostic and therapeutic value. It may be repeated up to three times a day, but must be started early when the blood is fluid.

Vigorous methods of artificial respiration are condemned; mucus should be removed from the child's air-passages, gentle traction made on the tongue, and coramine injected with the child in a warm bath. After recovery cyanosis is treated with oxygen and carbon dioxide. The intracranial pressure is reduced 10 per cent by rectal salines.

W. R. Winterton.

The American Journal of Obstetrics and Gynecology,

Vol. xxxi, No. 1.

Chronic hypochromic anaemia in women. L. A. Gray and M. M. Wintrobe.

A study of ovaries following the pre-operative administration of an extract of pregnancy urine. E. C. Hamblen and R. A. Ross.

The influence of collapse therapy in the treatment of pulmonary tuberculosis on menstrual physiology. E. M. Jameson.

*Vaccination during pregnancy as prophylaxis against puerperal infection. J. B. Bernstine and R. E. Otten.

Single contraction delivery in breech presentation. E. T. Rulison.

Water concentration of the blood during pregnancy, labour, and the puerperium. F. W. Oberst and E. D. Plass.

Pneumococcal pelvic infection in women. P. Tompkins.

*A study of the blood loss in the third stage of labour and the factors involved. J. B. Pastore.

The treatment of pelvic inflammation by iontophoresis of acetyl-beta-methylcholine-chloride. A. Jacoby.

A résumé of 223 cases of surgical sterilization. C. B. Lull.

The month of conception of 935 congenitally malformed individuals. D. P. Murphy.

Is the oval or female type of pelvis a rachitic manifestation? H. Thomas.

*Irradiation of the pituitary gland in the treatment of menopausal symptoms. C. G. Collins, E. P. Thomas, and L. J. Menville.

*Nembutal in the treatment of pre-eclampsia and eclampsia. J. W. Ross.

Cystitis emphysematosa. R. S. Rosedale.

Observations on the concentration of anterior pituitary-like hormone in the urine in chorion-epithelioma, with the report of a case. J. M. Linett.

The effect of sympathetic denervation upon ovulation and oestrus in the rat. H. G. Schwartz and C. L. Buxton.

Multiple arrhenoblastomata of the ovary. A. M. Gnassi.

On the origin of the amniotic fluid. H. Acosta-Sison.

Vaginal hernia of Douglas's cul-de-sac. R. J. Stearns.

Elliott's treatment in puerperal infection. J. H. Moore.

Personal record of hysterectomies performed during a period of five years. H. Grad.

A protective shield for prolapsed cord. W. F. Mengert.

Kirschner-Wagner operation for the construction of an artificial vagina. D. N. Barrows.

Arachnoidism in pregnancy. J. J. Hilton.

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VACCINATION DURING PREGNANCY AS A PROPHYLAXIS AGAINST PUERPERAL INFECTION.

Any suggestion or investigation that might decrease the number of cases of infection in the puerperium will always be seriously considered. That of increasing the resistance of the individual by vaccination has been advanced

by Bernstine and Otten. The morbidity of the two Amercan institutions concerned was 15.71 per cent and 22.32 per cent, with an average morbidity of 19.01 per cent. In a series of 51 vaccinated cases the morbidity was brought down to 5.9 per cent. In a large maternity hospital in the north of England the morbidity in 1934 among 2,019 patients who had attended the antenatal department was 4.8 per cent.

The vaccine was prepared from cultures of organisms obtained from the vaginae and cervices of pregnant women and from the cervices and blood of cases of definite puerperal infection. This mixed vaccine contained streptococcus haemolyticus, streptococcus veridans, staphylococcus aureus, bacillus coli communis, streptococcus nonhaemolyticus, and staphylococcus albus. Experiments were made with pregnant rats to test the reaction of the injection and to test the efficiency of the immunity obtained. A certain number of non-pregnant women were also vaccinated so that an exact knowledge of any possible reaction in the human being could be obtained before the vaccine was given to a pregnant woman. The 51 cases were accepted for vaccination irrespective of their past or present medical or obstetric histories; their acceptance depended only upon their willingness to co-operate. Thirty-four patients were multiparae and 12 of them gave a history of one or more complications during their previous pregnancies. Nineteen patients had one or more complications in the present pregnancy, including bad teeth, vaginal discharges, toxaemia of pregnancy, and pyelitis. Thirty-one patients had operative interference or one, or more, complicating features during the labour. The authors are of the opinion that this short series of cases, with a morbidity of 5.9 per cent as compared to the morbidity of the non-vaccinated cases of 19.01 per cent, proves the worth of this form of prophylaxis against infection.

A Study of the Blood Loss in the Third Stage of Labour and the Factors Involved.

Since using a method of estimating the blood test in the third stage of labour and described in a previous communication, Pastore has found an increase in the incidence of post-partum haemorrhage. He came to the conclusion that when the loss is not measured there is the tendency to under-estimate losses more than 450 cubic centimetres and to over-estimate losses less than 150 cubic centimetres.

In 500 consecutive cases there were 32 in which the blood loss was 600 cubic centimetres, or more—an incidence of 6.4 per cent. He found that the effect of the increase in blood lost was markedly to increase the incidence of sepsis and to prolong the stay in hospital. On analysing the cases in which the blood loss was excessive the author found that cardiac disease tended to increase the haemorrhage, but, contrary to expectations, myomata did not do so except in one case. Four out of 15 patients whose haemoglobin prior to delivery was less than 70 per cent had losses of 600 cubic centimetres, or more, and the author is of the opinion that it is important closely to follow the haemoglobin during antenatal supervision. Previous abortion, prolongation of the second and third stages of labour, breech delivery, premature rupture of the membranes, and operative delivery all tended to raise the incidence of a loss of more than 600 cubic centimetres. On the whole the author found no significant difference in the amount of blood lost in the

cases receiving analgesia as compared with those not doing so, but there were marked variations with the various forms of analgesia used. The highest incidence of haemorrhage, 12.5 per cent, was in cases treated with morphine and rectal ether; the incidence was fairly high with rectal ether alone, but it was markedly decreased when rectal ether was combined with scopolamine. Nembutal was not used on many occasions, but it did not increase the incidence of haemorrhage. He also found that ether anaesthesia alone gave an incidence of 33.33 per cent as compared with an incidence of 4.54 per cent with nitrous oxide alone. While discussing the management of the third stage, Pastore is of the opinion that the placenta should be expressed immediately after its separation, which can best be determined by noting the change of shape of the uterus from a flattened disc to that of a globe. He is also of the opinion that during expression of the placenta it is of the utmost importance not to push the fundus deeply into the pelvic cavity, as this increases the loss by obstructing the veins. He describes in detail his technique for the correct management of the third stage.

IRRADIATION OF THE PITUITARY GLAND IN THE TREATMENT OF MENOPAUSAL SYMPTOMS.

The authors state that irradiation of the pituitary gland gives a more marked relief from menopausal symptoms than any other type of therapy, and should always be advised in cases in which sedatives and hormone therapy have failed. They advise four exposures: on the first day through the right temporal region; on the second day through the left temporal region; and then a repetition of these two doses after an interval of three weeks. They treated 33 patients, only one of whom was neither relieved nor completely cured. They are of the opinion that this irradiation is accompanied by a disappearance of an excess of prolan in the blood and destroys the hypertrophied pituitary gland.

NEMBUTAL IN THE TREATMENT OF PRE-ECLAMPSIA AND ECLAMPSIA.

Ross reports a series of 35 cases of pre-eclampsia treated with nembutal, one capsule by mouth four times daily, none of which developed convulsions. Three patients treated without nembutal developed convulsions. In 24 cases of eclampsia nembutal promptly stopped and completely controlled the convulsions, whereas repeated injections of morphine failed to do so in two cases. He is of the opinion that nembutal is capable of preventing convulsions and is free of any possible harmful effect on organs already damaged.

CLINICAL AND PATHOLOGICAL DIFFERENTIATION OF CERTAIN SPECIAL OVARIAN TUMOURS.

Novak gives a short but excellent description of the main points of difference between the four special ovarian tumours, the disgerminoma, the arrhenoblastoma, the granulosa-cell tumour, and the Brenner tumour. This paper should be read by every surgeon and pathologist interested in gynaecology. He begins with a short description of the normal embryology of the ovary and goes on to explain the possible sources of origin of each tumour: (*a*) In the undifferentiated phase, when it is impossible to say

whether the gonad is going to develop along male or female lines, certain disgerminal cells may persist as rests and later may give rise to a tumour—the so-called disgerminoma. (*b*) The pro-testicular apparatus, which develops even in the gonad destined to be an ovary but is transient, may persist and form a tumour—the so-called arrhenoblastoma or masculinizing tumour. (*c*) The granulosa-cell tumour is said to arise from the unused granulosa cells of Pflüger's tubules which are concerned with the early formation of the primordial follicle. (*d*) The origin of the so-called Brenner tumour is more difficult to understand, but the author explains that probably it is derived from undifferentiated sex cells—the so-called Walthard cell nests.

The author also describes the chief clinical signs and symptoms of each of these tumours and gives an account of how they may be distinguished from each other histologically.

SUBPHRENIC COLLECTION OF LIPIODOL FOLLOWING ITS INJECTION INTO THE FALLOPIAN TUBES, WITH OBSERVATIONS ON REVERSE GRAVITATION OF PELVIC EXUDATES AND THE GENITO-PHRENIC SYNDROME IN WOMEN.

Rubin describes two cases, one of acute pelvic gonorrhoea and the other of an ectopic pregnancy with only very slight bleeding, in which the patient complained of pain in the region of the liver and shoulder. He is of the opinion that fluid in the lower part of the peritoneal cavity can gravitate upwards and can cause symptoms by irritation of the diaphragm. He terms this the genito-phrenic syndrome in women. The possibility of upward gravitation to the liver was further strengthened by the author's finding of a collection of lipiodol under the diaphragm in a case in which a Fallopian tube was injected with the oil during an abdominal exploration. The Fallopian tube ruptured during the manipulation and some oil was spilt in the pelvic cavity; the upper part of the abdomen had been completely packed off, so the chance of the oil passing upwards during the operation was negligible.

OPERATIVE TREATMENT OF URINARY INCONTINENCE.

Most gynaecologists will agree that one must give a guarded prognosis when operating for so-called stress incontinence. Douglass gives a good description of his technique in dealing with these distressing cases, and stresses the importance of a complete exposure and isolation of the neck of the bladder and upper part of the urethra. He inserts a mattress suture into the cellular tissues on each side over the front of the junction of the urethra and bladder and ties it with a catheter lying in the urethra. This usually effects a cure.

For the treatment of vesico-vaginal fistula which has resisted the usual methods of vaginal repair he advocates Young's transvesical operation. After opening the bladder the fistulous communication is invaginated by a finger in the vagina and a purse-string suture is inserted round the edge of the opening.

VESICO-VAGINAL FISTULA.

Although the obstetric vesico-vaginal fistulae have decreased Phaneuf points out that the surgical injuries of the bladder have increased because of

the greater number of surgical interventions involving the pelvic organs which are practised to-day. In the last 10,000 consecutive gynaecological and obstetric histories of his own patients he found 10 of these lesions—an incidence of one in 1,000. He advocates the use of silver wire in preference to catgut for the closure of all such fistulae because of the absence of inflammation and tumefaction around this material. He points out that in 1849 Sims, using silver wire on his thirtieth attempt in one case, was successful in closing the fistula.

He describes a series of 10 cases in which the accident was due to obstetric causes in four, to vaginal Caesarean section in one, and to surgical causes in five. One fistula was closed by the suprapubic extraperitoneal method after failure by the suprapubic intravesical and vaginal procedures. No fistula was successfully closed by the intravesical method, which was used four times. The vaginal method was responsible for the closure of the remaining nine fistulae. He used silver wire alone in three cases. In one case he used chromic catgut alone; the fistula persisted in this case, but was subsequently successfully operated on by another surgeon. In the remainder he used a combination of buried chromic catgut and silver wire for the vaginal mucosa.

STATISTICAL STUDIES ON PUERPERAL INFECTION.

Puerperal infection still ranks first in maternal mortality statistics and, as Peckham points out, is undoubtedly preventable. In this paper the author gives an account of the factors influencing the incidence of puerperal infection. He analyses a series of 5,767 consecutive cases delivered at, or near, term at the Johns Hopkins Hospital. Seven per cent were private cases; the remainder included those of the lowest social status—there were more black women than white. In this analysis he found that the incidence of infection was twice as high in the black patients, 20.24 per cent, as in the white, 11.05 per cent. A definite decline was noted in advancing age and parity of the patients, but in the first classification there was a slight rise in the higher age-group, probably the result of the greater risk of operative interference, and a very definite rise in the second group in women with nine, or more, children. As is to be expected the incidence was found to be two and a half times as frequent when the delivery was operative; the puerperium was febrile in two-thirds of the cases in which the placenta had to be manually removed. Prolongation of labour and blood loss, either before or after delivery, increased the incidence of infection by causing a lowering of general resistance. The death-rate from puerperal infection for Baltimore showed a seasonal variation similar to that observed for deaths due to respiratory diseases, except that the curve of the former followed the latter by about a month.

THE VASCULAR ASPECT OF ECLAMPSIA.

There are many theories for the cause of eclampsia, and Irving chooses the vascular theory as probably being the true one. He says that it is so essential to find a theory which embraces a common cause for all the signs and symptoms and the demonstrable changes produced in the body. The term "toxaemia" is condemned by him as no toxin has ever been isolated in eclampsia, nor is the blood of eclamptic patients more poisonous than that of other pregnant women. He advocates the theory that there is a spasm of

the arterioles which causes ischaemia of the organs. This affects the cells of the vessels' walls as well as the functioning cells of the organ concerned. When applied to the kidney, the clinical signs of albuminuria, oliguria, haematuria, and tubular casts can be explained on this theory. Fahr and others have demonstrated a swelling of the glomeruli with narrowing of the lumina of the vessels. It is a well-known fact that albuminuria can appear very suddenly, and this fact can only be satisfactorily explained by the presence of a sudden arterial spasm. On discussing the changes in the liver Irving quotes Acosta-Sison, who found that the haemorrhage, necrosis, and fatty degeneration occurred as much in the central and mid-zone areas of the lobule as in the periphery. This has been confirmed by many others. The finding of thrombosis of the radicles of the portal vein or of the small branches of the hepatic artery, together with those changes of the cells of the lobule, also places the hepatic lesions upon a vascular basis. In the brain, the fits can be accounted for by spasm of the vessels and by oedema of the cerebral tissue.

The author thinks that active steps should be taken to decrease oedema but that a raised blood-pressure may be a protective mechanism.

THE USE OF CORPUS LUTEUM IN THE TREATMENT OF DYSMENORRHOEA.

The authors use corporin, a product of pure corpus luteum hormone, and assert that it is necessary to have an extract completely free from follicular-stimulating hormone. They confined this form of therapy to cases in which the pelvic organs were normal. The dose was a daily subcutaneous injection of five to eight rabbit-units for five days prior to the onset of the menstrual period. It was found that the pain improved after the first course of injections, but complete freedom from pain was not obtained until three to five courses had been given. It was also noticed that it was always accompanied by an increase in the amount of the flow. The author explains that corporin is antagonistic to the action of the oestrogenic substance, which causes uterine irritability and painful contractions.

Bryan Jeaffreson.

The Journal of the American Medical Association

Vol. cvii, No. 11, September 12th, 1936.

*Carcinoma of the cervical stump. Lewis C. Scheffey.

Vol. cvii, No. 12, September 19th 1936.

*Delivery and care of the newborn infant of the diabetic mother. Lawrence M. Randall and E. H. Rynearson.

Rectal stricture complicating delivery. Cecil D. Gaines and James F. McDowell.

Vol. cvii, No. 13, September 26th, 1936.

Vascular collapse in toxaemia of pregnancy. Fred L. Adair, Arthur B. Hunt, and Rupert E. Arnell.

Vol. cvii, No. 15, October 10th, 1936.

Nomenclature of oestrus-producing compounds. Council on Pharmacy and Chemistry.

Vol. cvii, No. 16, October 17th, 1936.

Internal hernia following round ligament suspension. M. A. Michael.

Vol. cvii, No. 17, October 24th, 1936.

Clinical application of hormones of anterior pituitary and gonads (Editorial).

Vol. cvii, No. 18, October 31st, 1936.

*Studies in ovulation: the operative observations in periodic intermenstrual pain. Lawrence R. Wharton and Erle Henrikson.

Vol. cvii, No. 19 November 7th, 1936.

*The conservative treatment of abortion. James R. Reinberger and Percy B. Russell, junr.

CARCINOMA OF THE CERVICAL STUMP.

In reviewing the published statistics of the frequency of occurrence of stump carcinoma following supravaginal hysterectomy, the author concludes that the condition occurs in rather less than one per cent of cases. He believes that this danger does not justify total hysterectomy as a routine performance in every case, but advocates preliminary examination, curettage and biopsy of all cervices in cases in which hysterectomy is contemplated, with treatment of torn or infected cervices. He justifies this conservatism by quoting figures showing the greater operative mortality of the more radical operation, which more than discounts the risk of the development of stump carcinoma.

He describes the treatment of 10 cases of stump carcinoma with radium or X-rays, and obtained a five-year cure-rate of 42.8 per cent.

DELIVERY AND CARE OF THE NEWBORN INFANT OF THE DIABETIC MOTHER.

In spite of the great advances in the treatment of diabetes the death-rate of infants born to diabetic mothers remains high. The authors believe that this is due to several factors. Intra-partum deaths as term approaches are common, the foetus tends to be overlarge in relation to its maturity and may cause difficult labour, and the infant frequently suffers from marked hypoglycaemia at birth. As a counter to the first two causes of foetal death the authors advocate delivery of diabetic mothers by Caesarean section at the thirty-sixth or thirty-seventh week of pregnancy, and describe seven cases so treated.

The hypoglycaemia of the newborn infant is the result of continued overfunctioning of the islands of Langerhans. Especially towards term the foetal pancreas makes every effort to supply the insulin the mother lacks, with consequent hypertrophy of the islands of Langerhans. After birth the large amounts of insulin secreted by the child's pancreas result in a lowering of the blood-sugar that may cause death. To avoid this the authors suggest that the infant's blood-sugar should be estimated at birth, and that it should be raised to a normal level by early feeding and, if necessary, by the intramuscular injection of glucose. Asphyxia neonatorum is common in these cases and should be treated by the routine methods.

STUDIES IN OVULATION: THE OPERATIVE OBSERVATIONS IN PERIODIC INTERMENSTRUAL PAIN.

While the existence of periodic intermenstrual pain, or mittelschmerz,

has been recognized for many years, its origin has been variously assigned to uterine contractions, peristaltic movements of the Fallopian tubes carrying the ovum towards the uterus, and to ovulation itself. There is no doubt that the latter is the true explanation.

The authors present a series of 61 cases of this phenomenon, 30 of which were subjected to laparotomy. They found that the pain was remarkably regular in its recurrence, in the majority of cases occurring between the tenth and twelfth days of the menstrual cycle. It is usual for the symptoms first to appear in young women, often dating from the onset of menstruation. The pain varies greatly in severity, from mere pelvic discomfort to agonizing cramps. The most acute type frequently has no previous history of the condition, and this renders the diagnosis the more difficult, especially as the pain may be accompanied by pyrexia and leucocystosis. The condition is not associated with dysmenorrhoea or sterility, and curettings of the endometrium appear normal.

The chief differential diagnosis is from appendicitis or salpingitis, though bleeding from the follicle may be sufficiently severe to simulate ruptured ectopic gestation. At operation a recently ruptured follicle was almost invariably found, and excision of this was the routine procedure. The authors believe that unilateral oöphorectomy is unjustifiable, as there is no probability of this curing the condition. Hysterectomy and presacral sympathectomy do not relieve the pain, but the latter disappears, as would be expected, during pregnancy and after the menopause. In some cases the condition is of a temporary nature, and this fact probably accounts for the cures which occasionally follow such procedures as curettage of the uterus or even rest in bed. The authors suggest that the painful ovulation is due to some change, often temporary, of an inflammatory or circulatory nature.

THE CONSERVATIVE TREATMENT OF ABORTION.

In an analysis of 707 cases of abortion admitted to the John Gaston Memorial Hospital the authors find that of the 518 incomplete cases only 18, or 3.5 per cent, required intra-uterine operations. The majority were treated conservatively, oxytocic drugs being administered when bleeding was profuse or prolonged. In febrile cases active intra-uterine manipulation was not attempted if the infection had spread beyond the uterus, this procedure being reserved for cases of incomplete abortion in which bleeding continued after the administration of oxytocics, or in which sepsis was limited to the uterus itself.

Blood-transfusion was given to the majority of patients with red-cell counts of less than 3,500,000. The deaths in the whole series totalled nine, three of the patients being moribund on admission.

F. H. Finlaison.

Surgery, Gynecology and Obstetrics.

Vol. lxiii, No. 2, August 1936.

*The response of the mammary gland to prolonged stimulation with ovarian hormones. I. G. Macdonald.

*Ovarian function and the occurrence of menopausal symptoms following hysterectomy. R. Mark and B. J. McKennon.

*Prophylaxis in gynaecology; with special reference to the immediate care of the post-partum cervix. B. H. Goff.

*Pelvic abscess in women; complications and management with a study of 328 cases. D. R. Jensen.

Vol. lxiii, No. 3, September 1936.

*The use of catgut in the perineum. O. W. Hess.

*The surgical management of prolapse of the uterus and vagina. L. E.

*The cystocele; its anatomical disturbance and reconstruction. J. W. Davies.

*The surgical management of prolapse of the uterus and vagina. L. E. Phaneuf.

Vol. lxiii, No. 4, October 1936.

*Toxaemais of pregnancy. J. R. Goodall.

*Treatment of trichomonas vaginalis and trichomonas in the male. E. L. Cornell and L. W. Riba.

Vol. lxiii, No. 5, November 1936.

*Intervals between pregnancies of mothers giving birth to congenitally malformed children; a study of 531 families. D. P. Murphy.

*The production of vaginal activity by oestrin; its importance in the treatment of gonorrhoeal vaginitis. R. M. Lewis and L. Weinstein.

Vol. lxiii, No. 6, December 1936.

*Endometrial histology and pathology as revealed by the biopsy method. R. E. Campbell, F. C. Lendrum, and E. L. Sevringhaus.

*The vesical complications of carcinoma of the cervix. R. C. Graves, C. J. E. Kickham, and I. T. Nathanson.

THE RESPONSE OF THE MAMMARY GLAND TO PROLONGED STIMULATION WITH OVARIAN HORMONES.

The author has carried out experiments to show the changes which can be produced in the mammary gland by long periods of artificial stimulation with progestin. The continuous administration of oestrin in castrated rabbits produced, at first, a generalized overgrowth and ramification of the ductal system in the mammary gland with practically no acinar growth. Carried further, little gross change occurred but atypical histological variations appeared in the ductal epithelium, which were often on the border-line of neoplastic changes. Prolongation of this stimulation for six months or more produced a state of regression of ductal growth and epithelial hyperplasia.

A combination of oestrin and corpus luteum extract produced both ductal and acinar overgrowth; early secretion occurred and the ducts became distended.

Oestrin and progestin did not produce specific pathological lesions, cystic disease and adhesions in so far as the author's investigations were carried.

OVARIAN FUNCTION AND OCCURRENCE OF MENOPAUSAL SYMPTOMS FOLLOWING HYSTERECTOMY.

The authors have investigated 21 cases in which total or supravaginal hysterectomy had been performed with the preservation of as much ovarian

tissue as seemed advisable, both, or at least one, of the ovaries being retained.

It was found that there was a noticeable contrast between the hormonal picture and occurrence of hot flushes following total and supravaginal hysterectomy. The hormonal picture and clinical symptoms of the menopause appear earlier and are more marked after total hysterectomy than after supravaginal hysterectomy.

The preservation of even a small part of the uterus seems to have a retarding and mitigating effect upon the appearance of retrogressive changes in the pituitary-ovarian function and the occurrence of menopausal symptoms.

It was found that the output of oestrin after hysterectomy is determined more by the biological quality than by the amount of ovarian tissue retained.

The occurrence of hot flushes after hysterectomy was found to be associated with an increase of prolan and a decrease of oestrin in the majority of cases.

PROPHYLAXIS IN GYNAECOLOGY, WITH SPECIAL REFERENCE TO THE IMMEDIATE CARE OF THE POST-PARTUM CERVIX.

This paper has been written primarily to stimulate interest in a neglected gynaecological procedure, namely, primary trachelorrhaphy as a prophylactic measure against chronic cervical infection.

In the present series the incidence of cervical lacerations of 0.5 centimetre, or more, in extent was 30 per cent in primiparae and 15 per cent in multiparae. The author states that lacerations of 1.5 centimetres, or more, in extent should be corrected immediately after the third stage of labour by primary trachelorrhaphy and post-partum haemorrhage from such lacerations should likewise be controlled by trachelorrhaphy. The procedure should not be employed in infected cases except for the control of haemorrhage.

Although the results of immediate trachelorrhaphy are not ideal, it is an invaluable prophylactic procedure against post-partum cervical infection and its sequelae, but it should not be practised by any other than a competent obstetrician who is trained in the art of plastic vaginal surgery.

PELVIC ABSCESS IN WOMEN: COMPLICATIONS AND MANAGEMENT, WITH A STUDY OF 328 CASES.

The author has presented a study of 328 cases of pelvic abscess in women; 197 of these patients were in the Women's Hospital, New York, and 131 in the Bellevue Hospital, New York.

In the first group, after posterior colpotomy alone, 36 patients had a thickening in the pelvis, 44 had a mass with induration, and in 23 the findings were negative. After abdominal operation combined with posterior colpotomy, three patients had pelvic thickening, three a mass with induration, and in 33 the findings were negative. In the Bellevue group nine patients had a mass with induration after posterior colpotomy, while 37 had only thickening.

Fifty-one patients were readmitted one, or more, times at the Women's Hospital, 33 of the patients had recurring collections of pus, and 15 had

posterior colpotomy for drainage. In 18 abdominal operation was done with excision of the wall of the abscess, complete closure of the incision and drainage by posterior colpotomy. Laparotomy was performed in 13 for separation of adhesions and excision of chronically thickened tissue. In eight operation was unnecessary, the symptoms subsiding after rest in hospital. Other readmissions were: one ectopic pregnancy, one carcinoma of the rectum, one carcinoma of the cervix, and two for the treatment of menorrhagia. The rest of the patients in this group were readmitted for conditions unrelated to the previous pelvic disease.

There were 12 readmissions in the Bellevue group: three had drainage by posterior colpotomy for recurrent abscess, an abdominal operation was performed on three for excision of a pus sac with drainage through the abdominal incision, in five there was no operation, and one patient entered because of a miscarriage.

The results of treatment were variable, but in general the more conservative the measures the less the morbidity, and the more extensive the operative interference the higher the mortality.

THE USE OF CATGUT IN THE PERINEUM.

The author has made several experiments with catgut in the perineum. In the first group various sizes of plain and chromic catgut were embedded in the perineum and later removed at indefinite intervals for testing on the tensile strength machine. In the second group observations were made *in vitro* regarding the effect of the lochia upon catgut, and for a comparison of effect similar studies were carried out *in vitro* by first immersing the sutures in normal saline solution and in sterile serum.

The results of the first group showed that the tensile strength of catgut undergoes rapid and progressive diminution commensurate with the duration of time that the gut remains in the tissues. When the catgut was immersed in saline, serum or lochia, the moisture had little effect and there was comparatively little loss of strength when the suture was dried and tested.

Despite the fact that catgut embedded in the perineum loses strength at a rapid rate, observations are recorded by the author which indicate that when certain conditions are fulfilled, more satisfactory healing of wounds occurs when finer sizes of catgut than are commonly recommended are employed.

THE CYSTOCELE: ITS ANATOMICAL DISTURBANCE AND RECONSTRUCTION.

The bladder, like the vagina, is suspended in the centre of a sling which is made up of blood-vessels and nerves supplying the organs. This structure is essentially a mesentery, but being devoid of a peritoneal coat could more descriptively be called a mesenteroid than a ligament. The paravesical layer on the vaginal surface of the bladder is intimately attached to the bladder and has been called the pubocervical ligament, which acts as the anterior support of the cervix and also as a shelf for the base of the bladder. A dilating cervix stretches and may tear its anterior cervical attachments. During the second stage of labour the bladder is displaced anteriorly, and the displacement may overstretch or tear the area between its lateral mesenteroids. A cystocele may result from the over-stretching or tearing of

the thin preperitoneal layer on the base of the bladder. Tightening this tissue from side to side reconstructs the damage to the base of the bladder and increases the tone of the lateral mesenteroids. It is not necessary to remove the redundant vaginal layers accurately after the completion of the reconstruction of the bladder, because the involuntary muscular coat will adapt to a normal contour. The author is of the opinion that embarrassing strictures or undercorrected cystoceles will be fewer if the thin preperitoneal tissue on the base of the bladder is utilized in performing the operation.

THE SURGICAL MANAGEMENT OF PROLAPSE OF THE UTERUS AND VAGINA.

During a period of 22 years the author has operated on 382 women for prolapse, and he has tried most of the procedures in common use.

Utero-vaginal prolapse in young women during the child-bearing age may be satisfactorily treated by repairing the cervix, the anterior and posterior vaginal walls, the perineum, by shortening the utero-sacral ligaments and by suspending the uterus to the anterior abdominal wall by the round ligaments. After the menopause it is preferable to use a vaginal method. The operation most frequently employed by the author is the interposition operation followed by amputation of the cervix. Vaginal hysterectomy with interposition of the united broad ligaments should be used in patients with atrophied uteri and when malignant disease is suspected. In older women, when an extensive vaginal operation is contra-indicated, Le Fort's operation, or total colpectomy may be found most useful. An adequate repair of the pelvic floor is essential in all cases, except in nulliparous prolapse when the perineum is intact.

TOXAEMIA OF PREGNANCY.

The author has been studying the toxaemias of pregnancy during the last two or three years, and he has reached some interesting conclusions.

Briefly, for purposes of treatment his cases were grouped as acute and chronic, the former including eclampsia.

In acute cases the author is of the opinion that the whole object of treatment should be to allay nervous irritability and promote elimination. Sedatives should be used, morphine usually being the most handy, but luminal, sodium amytal, nembutal and avertin can all be used with caution. If the blood-pressure is high and there is any sign of papillary oedema or severe headache, the author advocates bleeding followed by a small amount of intravenous hypertonic solutions of sugar, sodium chloride or magnesium sulphate. The injection should be the equivalent of about one-quarter of the blood withdrawn. This promotes a return of the excessive extra-vascular cell plasma into the blood-vessels, and a general relief of cell pressure, and, of far greater importance, relief of the pressure on the cerebral neurones. The patient should be put on a strict diet at first, later milk, carbohydrates and vegetables may be added.

Turning to albuminuria of pregnancy, the author describes his plan of action as follows. In primiparae with severe eclampsia and a closed cervix Caesarean section is indicated. In multiparae the history of past labours must be given consideration. If there is a history of easy and rapid labours, rupture of the membranes will suffice, giving due consideration to

the severity and frequency of the attacks, and to the facial appearance. If the obstetric history is bad Caesarean section is again indicated.

In the group of chronic cases there is ample time to give the case considerable thought, while the patient is made to rest and kept on a strict diet. Besides the primary study of the mother, the prospect of the unborn child must be considered, the economic and social status, the absence of children or the presence of many; everything related to the case should be weighed carefully. The doctor, knowing that in chronic cases the longer the prenatal hypertension lasts the greater is the likelihood of its persistence afterwards and its ultimate result upon the organs, should place this fact and that of the child's life being in danger, before the parents. He is then free to act with the sanction of the parents, but such a decision must rest with those intimately concerned after every contingency known to science has been placed in rational balance.

Treatment of Trichomonas Vaginalis.

Cornell and Riba have been using devegan in the treatment of trichomonas vaginalis. Their technique is as follows. The vagina is cleansed with cotton pledgets. Three tablets are placed around the cervix and the speculum is removed. The patient reports three times a week before and during the next menstrual period; thereafter each night the patient inserts one tablet high up in the vaginal vault. The patient returns to the doctor on the first day of each period and every other day during the period, for four menstrual cycles, at which time the vagina is cleaned and three tablets are inserted. After the fourth period no medication is used and a week later a smear is taken. If the result is negative she returns after the next period having had no treatment, and if none is found this time she is pronounced cured.

The husband should be examined to exclude the possibility of his being a carrier. This done, he is instructed not to have intercourse without condoms until his wife is pronounced cured. Natural intercourse is permitted after the fifth period if the vaginal smears are negative. The patient returns for examination a week to 10 days after this sexual intercourse, and if the smears are positive, she is considered to have been infected by her husband and is subjected to further examination.

The authors have treated 25 women, and the results are not universally known, but seven were pronounced cured and five discontinued treatment. Seven were pregnant at the time treatment was commenced, and in these patients they were only able to control the discharge. The authors are not prepared to state that devegan will cure this condition more promptly than any other of the recognized drugs, but they hope to make a further report.

Intervals between Pregnancies of Mothers giving Birth to Congenitally Malformed Children, a Study of 531 Families.

The lengths of the non-pregnant intervals were determined for 2,146 pregnancies which occurred in a consecutive series of 531 families. Of the 2,146 pregnancies, 584 terminated in the birth of congenitally malformed children and 1,562 in the birth of their normally developed brothers and sisters.

The non-pregnant intervals preceding the conceptions of 584 congenitally malformed children were found to be significantly longer than the same intervals for their 1,562 normally developed brothers and sisters.

This obsevation leads the author to believe that mothers of congenitally malformed offspring are wont to experience a more or less prolonged period of reproductive inefficiency at the time that their congenitally malformed offspring are born.

THE PRODUCTION OF VAGINAL ACIDITY BY OESTRIN.

The successful results reported in the use of oestrin in the treatment of gonorrhoeal vaginitis in children, aroused the authors' interest and led them to try to determine more definitely the manner in which a gonococcal infection is terminated by a temporary change in the vaginal mucosa as a result of endocrine therapy.

They found that the acidity of the vaginal secretions is easily measured and gives easily obtained reliable proof that oestrin therapy has brought about the desired histological reaction of the vaginal mucosa. Doederlin's organism was present only in a few of the children examined, and its presence or absence could not be correlated with the acidity or alkalinity of the vaginal tract.

ENDOMETRIAL HISTOLOGY AND PATHOLOGY AS REVEALED BY THE BIOPSY METHOD.

The authors have written this paper in order to point out the characteristic manifestations produced in the endometrium by the follicular hormone and the hormone of the corpus luteum, and to recommend the examination of the endometrial histology by the biopsy method as a control for endocrine diagnosis and therapy.

Endometrial biopsy causes only minimal disturbance to the patient, and it is possible to obtain several endometrial specimens during a single cycle. It is, therefore, a useful procedure in determining what endocrine disturbance, if any, may be the cause of such a condition in amenorrhoea, menorrhagia, or sterility.

Endometrial biopsy is not yet an adequate substitute for a good clinical history, as amenorrhoea, cyclical follicular bleeding, and menorrhagia are indistinguishable on the basis of endometrial histology.

THE VESICAL COMPLICATIONS OF CARCINOMA OF THE CERVIX.

The bladder is frequently involved in cases of carcinoma cervicis, either by the disease itself or as the result of treatment. It is well known that the more advanced the local disease, the greater the likelihood of vesical invasion, but it is difficult to determine the extent of the disease by pelvic examination alone. Cystoscopic examination may be just as important as pelvic or pathological examinations in determining the true state of affairs.

The proliferative type of growth is likely to produce at cystoscopy the picture of extra-vesical pressure. Some tumours of this type extend to the bladder, but submucous infiltration of the vagina usually precedes this extension.

The ulcerative type of growth possesses a greater tendency to vesical

invasion than others. It is distinctly destructive, and once the cervix is partially destroyed, continuation in the bladder may easily follow.

The invertive, or endocervical, type seldom spreads towards the bladder, but here, too, one may see evidence of the tumour by cystoscopy. This form of tumour may be confined to the cervix for a relatively long time before extending into neighbouring structures. The vesical changes due to radiation are usually late and seldom progress to fistula.

In every instance of late radium reaction in the bladder in this series, radium seeds—occasionally glass, but usually gold—were used in the treatment of the cervix. The authors believe this to be of great significance, since inadequate filtration and the site of insertion in the periphery of the growth, undoubtedly play the greatest part in the production of this sequela.

The authors stress the fact that extension of disease into the bladder from the cervix should not be a deterrent to vigorous treatment of the malignant process. They quote a case in which the patient had such extension even to the point of vesico-vaginal fistula at the time of the first examination and who now, after treatment, presents no evidence of active carcinoma. The fistula remains, but they consider this is not too high a price to pay for successful cure.

C. D. Read.

La Gynécologie.

February 1936.

*Concerning the causes of premature labour and the prognosis to the foetus born before term. Folke Holtz.

Submucous uterine fibromata and the puerperium. S. Klein.

Transactions of the Obstetric and Gynaecological Society of Paris. June 1935.

August 1936.

*Concerning the ovarian graft. The antenatal conditions for the conservation of the ovary *in situ*. The blood-supply of the ovary. Massabuau, Guibal, and Joyeux (Montpelier).

*Haemorrhages of the ovary. An anatomical and pathological investigation. A. Picaud.

The Fifth French Congress of Gynaecology. Paris. May 1936.

Concerning the Causes of Premature Labour and the Prognosis to the Foetus Born before Term.

The author points out the difficulty of deciding whether or not a foetus is premature. Some suggest that length should be the deciding factor, and use 47 centimetres as the low limit at term; others use the weight, 2,500 grams being the low limit for this at term. The author shows the fallacies of these methods; and in his series he has counted as premature all those which present one or more signs of imperfect development, such as reddish skin, lanugo, nails not reaching to the ends of the fingers, a feeble and plaintive cry, even if the length is greater than 47 centimetres and the weight greater than 2,500 grams. On the other hand he has

excluded cases in which labour occurred at the fortieth week, when the length and weight were, respectively, less than 47 centimetres and 2,500 grams, but when the signs of development were perfect.

The series consists of 313 premature deliveries in 5,821 cases. The author, after analysing his figures, shows (1) that the frequency of premature labour is 5.12 per cent. (2) That premature labour does not occur more often in primigravidae than in multiparae. (3) That, perhaps, the frequency is a little higher in single than in married women. (4) That age has little to do with premature labour. (5) That abnormal presentations, especially breech presentation, occur more frequently. (6) That the abnormal presentation of a twin is caused mainly by the conditions present in a twin pregnancy, i.e. not prematurity.

In discussing the aetiology the author divides the material into the following groups: (1) Spontaneous premature labour following (*a*) detachment of the placenta (21.24 per cent), (*b*) dead foetus (8.17 per cent), (*c*) abnormal distension of the uterus (17.32 per cent), (*d*) premature rupture of the membranes (11.76 per cent), (*e*) placental infarcts (15.36 per cent), (*f*) unknown factors. (2) Induced premature labour.

There were 65 cases in which the detachment of the placenta was the cause of premature labour. In 35 of these the placenta was on the lower uterine segment; of the remaining 30, 20 were due to toxaemia, two were syphilitics, and one was a case of chronic nephritis.

In 39 cases the foetus was dead before labour commenced; but 14 of these were due to detachment of the placenta. Of the remaining 25, large placental infarcts were found (of which seven were due to toxaemia), one mother had a severe cardiac lesion, and another had severe toxaemia without a placental lesion. For the other deaths compression of the cord was suggested as a possible cause.

In 53 cases abnormal distension of the uterus was considered the main cause of premature labour. Ten of these had early rupture of the membranes, six were due to toxaemia, 17 were cases of hydramnios, and 36 were cases of twins. In the 78 twins of the series 41 were premature, but in three cases detachment of the placenta was considered the cause, and in two cases a dead foetus.

Early rupture of the membranes was considered the chief factor in 36 cases, although in six of these toxaemia was present. The time between rupture of the membranes and the beginning of labour varied from five hours to 19 days.

Placental infarcts were considered to be the cause in 47 cases, and of these 13 were co-existent with toxaemia of pregnancy. In 80 cases no lesions were found to which the author could attribute the premature labour. Fifteen of these were cases of toxaemia or of chronic nephritis, but no placental lesions have been noted. Most of these 80 cases were near to term. It is interesting to note that toxaemia was present in 18.63 per cent of the cases, and nephritis in 3.92 per cent of the cases.

In seven cases premature labour was induced artificially because of eclampsia or eclampsism, in three cases the membranes were ruptured, and in four Caesarean section was performed. The author also shows that separation of the placenta and foetal death are factors occurring relatively more often in the early premature labours, while abnormal distension,

premature rupture of the membranes and placental infarcts occur more often in the late premature labours.

The foetal prognosis is, of course, bad. When the foetus weighed less than 2,000 grams, 21.23 per cent were dead before delivery, 8.22 per cent died during delivery, and 39.73 per cent died after delivery. When the foetus weighed more than 2,000 grams the corresponding figures were 3.85 per cent, 2.88 per cent, and 10.58 per cent. For the survivors the figures were 30.82 per cent under 2,000 grams, and 82.69 per cent over 2,000 grams.

CONCERNING THE OVARIAN GRAFT. THE ANATOMICAL CONDITIONS FOR THE CONSERVATION OF THE OVARY *in situ*. THE BLOOD-SUPPLY OF THE OVARY.

The authors consider that the menopausal disturbances following surgical castration warrant every effort to conserve the physiological integrity of woman, especially the maintenance of the ovarian function. They suggest that the modern tendency is to transplant the ovary. They ask whether the vitality of the ovary is compromised in pelvic operations, what are the causes of the same, and what are the conditions which will assure the integrity of the ovary. They have tried to decide what arterial supply must remain in order that the ovary may be intact; or which comes to the same thing, which pedicles may be ligatured without causing atrophy, degeneration or necrobiosis of the ovary.

They do not ignore the role of the nervous system or of the uterine mucosa, but suggest that an intact blood-supply is of major importance. The ovary has two arteries of supply, and it is interesting to know which part each has to play in the distribution of the arterial blood to the genital gland. Some authors stress the importance of the uterine artery, some the ovarian, and some the anastomosis between the two.

Is the blood-supply of the Fallopian tubes independent of that of the ovaries? Can salpingectomy be performed without injury to the ovary? The authors have investigated these points by means of dissection, injecting the arteries with coloured wax and by arteriography, using lipiodol, in subjects from a foetus at the fifth month of intra-uterine life to the menopause.

The results. There are two types of blood-supply. (1) Foetal. During foetal life the uterine artery supplies at least the inner pole of the ovary; the ovarian artery the outer pole; and the middle segment is supplied by the great anastomotic arch between the uterine and ovarian vessels. (2) Adult. Near the cornua the uterine artery sends off two branches, a large principal anastomotic artery and a smaller anastomotic artery. The ovarian artery divides into two branches, the principal anastomotic branch and the tubo-ovarian branch which divides into three, the tubal supplying only a small branch to the ovary, the ovarian branches, and the secondary anastomotic. So there are three anastomoses, the principal utero-ovarian anastomosis below the ovary, the secondary utero-ovarian anastomosis on a level with the ovary, and the small sub-tubal anastomosis.

Which artery plays the greater part? The uterine artery has a greater calibre than the ovarian. From the point of view of distribution, the ovarian seems the more important. Practically, however, the authors point to the importance of the anastomotic arch, and that the uterus is normally removed in such a way as to leave one branch of this arch which is sufficient

to supply the ovary. They have also shown that the Fallopian tube may be removed without injury to the ovarian blood-supply.

Conclusions. The blood-supply of the ovary is assured by the anastomotic arch, and so long as one branch of this is left the ovary will be undisturbed. Operations designed to remove the uterus without interfering with the uterine trunk are not justified because of their complexity. The Fallopian tube is supplied by an independent system, and can be removed without interfering with the ovarian supply, so long as the arteries are ligatured individually. Diagrams are given.

HAEMORRHAGES OF THE OVARY. AN ANATOMICAL AND PATHOLOGICAL INVESTIGATION.

The author divides the ovarian haemorrhages into seven groups: (1) Interstitial, (2) intra-parenchymatous, (3) cystic, (4) multiple, (5) parietal, (6) haemorrhages into tumours, (7) haemorrhages from an ovarian pregnancy. The author has based his observations on two series of 106 cases of macroscopic or microscopic haemorrhages in the ovary. In one series the interstitial haemorrhages formed 39 per cent, and in the second 25 per cent. In some cases these were coincident with intraparenchymatous, cystic and parietal bleeding, but in more than half of them the bleeding was only interstitial, thus proving that ovarian haemorrhages may be primarily interstitial. He also suggests that the bleeding follows a change in the permeability of the capillaries due to the action of surrounding tissue.

The intraparenchymatous bleeding can be placed into three groups: (1) Haematoma of the Graafian follicle, (2) bleeding at ovulation, (3) haematoma of the corpus luteum. Haematoma of the Graafian follicle is rarely mentioned in the literature, and only two cases of peritoneal bleeding due to this have been reported. The author has seen nine haemorrhages into immature follicles.

Several haemorrhages at ovulation are reported, but the author doubts most of them. He considered two. In one the bleeding is said to come from a vein near the stigma, and in the other the diffusion of blood is such as to prevent the origin being defined. Normally the corpus luteum contains a nucleus of blood-clot. The time at which this is produced is not agreed on, but the author supports those who state the time of production to be menstrual, since before menstruation he finds no clot in the corpus luteum, nor in specimens removed during pregnancy. He defines this bleeding as abnormal when there is dissociation of the lutein tissue with an absence of the limiting membrane between the lutein layer and the haemorrhagic zone.

Taking this definition, haematoma of the corpus luteum formed 13 per cent of his cases. Histologically he has distinguished cases of haematomata of the recent corpus luteum, of the old corpus luteum, and of the restiform body. He has also seen bleeding into the layers of the corpus luteum, perilutein and perithecal. In many cases these lesions are accompanied by severe intra-peritoneal bleeding. He divides the cystic haemorrhages into three groups: haemorrhages into cysts, intra-peritoneal haemorrhages becoming cystic, such as endometriomata, and interstitial haemorrhages forming pseudo-cysts. He point out that in most cases microscopical examination is necessary to distinguish between haematoma of the follicle

and haematoma of the corpus luteum in different stages of development or degeneration.

Multiple haemorrhages are often found, sometimes of different types. In six cases of the series infection played an important part.

Haemorrhages are common into such ovarian tumours as pseudo-mucinous cyst adenomata, serous cyst adenomata, dermoids, follicular cysts, cysts of the corpus luteum, malignant ovarian growths and Brenner's tumours.

In ovarian pregnancies, 99 of which have now been reported, intra-abdominal haemorrhage is nearly always present. In the 106 cases the ovarian bleeding was intra-follicular in six per cent, intra-lutein in 25 per cent, intra-cystic in 51 per cent, parietal in 15 per cent, and interstitial alone in four per cent.

Interstitial haemorrhages occurred in 25 per cent, multiple haemorrhages in 20 per cent. In 15 per cent of the series there was intra-peritoneal bleeding. In 25 per cent of ovarian tumours haemorrhages occur.

R. Newton.

Gynécologie et Obstétrique

Vol. xxxiv, No. 3, September 1936.

Frontal naevi of the newborn. Fruhinsholz, Hartemann.
Tuberculosis of the body of the uterus. N. C. Lapeyre and H. Guibert.
Invasion of the upper part of the pelvis by the trichomonas vaginalis. E. Hees.
Trichomonas vaginalis and leucorrhoea. G. Tempé.
*Thoracoplasty and pregnancy. A. Blisnjanskaja and A. Laserevitch.

Vol. xxxiv, No. 4, October 1936.

The late results of ovarian grafting with conservation of the uterus. G. Cotte.
*Surgical closure of the pouch of Douglas (Marion's operation). G. Cotte.
*The action of testosteron acetate on the sexual cycle of the rat and the genital tract of the rabbit. G. Cotte and R. Noel.
*The action of di-hydro-folliculin on plants. Cl. Meyer.
Premenstrual pyrexia in pulmonary tuberculosis. R. Weiller.
The formation of an artificial vagina by Baldwin's operation. A. Gridnew.

THORACOPLASTY IN PREGNANCY.

The author reviews 12 published cases of pregnancy following thoracoplasty for pulmonary tuberculosis and describes seven personal cases from a Moscow clinic. In each case the operation had proved successful in arresting the disease and the pregnancy, commencing at periods from two to six years after it, was well tolerated and labour normal.

They conclude that pregnancy should be allowed to continue in such cases, provided that the disease is arrested and the environment of the patient satisfactory. On the other hand, if thoracoplasy has failed, a subsequent pregnancy should be terminated. Operative delivery is advised to avoid strain in the second stage of labour.

SURGICAL CLOSURE OF THE POUCH OF DOUGLAS.

Cotte reviews 80 cases in which he has performed Marion's operation. He uses a series of three or four superimposed purse-string sutures to close the pouch of Douglas, taking especial care not to encroach on the posterior surface of the uterus with the uppermost stitch. This precaution ensures that the uterus will not be forced into a position of extreme anteversion. It is important not to kink the Fallopian tubes or leave any peritoneal pouches or apertures which may occasion subsequent strangulation. The most likely site for these to be left is on the right side of the rectum, and, in closing the fossa in this situation care must be taken not to injure the ureter or the hypogastric vessels as they lie near the peritoneal surface.

The commonest indication for the performance of the operation is retroversion, in many instances of which the author considers it sufficient without the aid of an additional suspension. Perhaps its greatest value lies in cases of prolapsed ovaries.

THE ACTION OF TESTOSTERON ACETATE ON THE SEXUAL CYCLE OF THE RAT AND THE GENITAL TRACT OF THE RABBIT.

Experiments by Cotte and Noel with testosteron acetate may be summarized as follows: (1) In two normal rats with normal sexual cycles the injection of a total of 1.25 milligrams of testosteron acetate over a period of nine days produced complete arrest of the cycle with suppression of all follicular activity. (2) In a series of castrated rats the injection of testosteron acetate failed to induce the changes of oestrus. (3) In castrated rabbits, initially treated with folliculin, the injection of testosteron acetate did not produce the histological changes in the uterus and breasts noted when an extract of the corpus luteum is used after folliculin. In animals treated successively with folliculin and progestin the further injection of testosterone did not maintain the secretory changes.

The authors conclude that, despite its close chemical affinity with folliculin and progestin, testosterone has very different biological effects.

THE ACTION OF DI-HYDRO-FOLLICULIN ON PLANTS.

Meyer has observed the action of dilute solutions of di-hydro-folliculin on the growth of plants under careful experimental conditions. In the first experiment Indian corn was grown in an artificial soil of known constitution. The different solutions with which the plants were watered were all adjusted so as to have a *p*H of 7.5 None of the plants watered with the solutions of di-hydro-folliculin grew as well as the controls. Those watered with solutions containing one milligram of the drug to 20 litres of water grew better, however, than those receiving a solution 10 times as strong, i.e. one milligram to two litres. The plants were subsequently transplanted to normal soil. The treated plants ripened unduly quickly, and produced very few grains as compared with the controls.

Similar results were obtained in the second experiment in which barley was used. They found a type of necrobiosis in the roots of the plants receiving the drugs.

These results do not accord with much of the published work, a discrepancy due in the author's opinion to a frequent failure to use chemically pure reagents under strict experimental condiions.

P. Malpas.

Bruxelles Medical.

Vol. xvi, No. 45, September 6th, 1936.

*Hypophyseal irradiation in the treatment of pregnancy oedema. Georges Lambert.

Vol. xvi, No. 46, September 13th, 1936.

*The aetiology of senile vulvo-vaginal pruritus and its rational treatment with folliculin. J. A. Schockhaert.

Vol. xvi, No. 47, September 20th, 1936.

Ten years' experience in the sterility clinic in the Maternity Hospital of Lariboisière. Louis Devraigne.

*Clinical and biological considerations regarding extra-uterine gestation. R. Bourg.

Vol. xvi, No. 48, September 27th, 1936.

A case of gynaecomastia. R. D. G. Ph. Simons.

A large cervical fibromyoma. Kridelka.

The Second International Congress of the Scientific and Sociological Fight against Cancer. (Report of Proceedings.)

*Streptococcal infection of unknown origin in a woman eight months pregnant. J. Bernard.

The Second International Congress of the Scientific and Sociological Fight against Cancer. (Report of Proceedings, *continued*.)

Vol. xvi, No. 50, October 11th, 1936.

*Rupture of extra-uterine gestation due to folliculin. Vanderzypen.

The Forty-fifth French Congress of Surgery, October 5th to 10th, 1936. (Report of Proceedings.)

Results of ovarian grafts. P. Mocquot and G. Cotte.

Vol. xvi, No. 51, October 18th, 1936.

Re-infection with syphilis. J. Pierard.

*Conversion of mento-posterior positions into occipital presentations. O. Dawe.

HYPOPHYSEAL IRRADIATION IN THE TREATMENT OF PREGNANCY OEDEMA.

The view is expressed that disturbance of posterior pituitary function is a more likely cause of pregnancy oedema than are metabolic disturbances and other factors which have been blamed in the past. Strong clinical and experimental evidence in support of this view is reviewed. The posterior hypophysis, or the hypothalamic-hypophyseal complex, not only controls water balance but affects the mineral contents of blood and tissues.

Patients, of whom the author gives the details of four, were given a diet containing known amounts of water, protein and salts. Their weight, urine output and blood chemistry were then investigated before and after subjecting their posterior pituitaries to X-rays. Each patient received six treatments at intervals of two days, the total dosage being 1,100 international rat-units.

The author concludes that hypophyseal irradiation tends to mobilize the chlorides from the tissues to the blood-stream and increases the output of fluid from the body, thus reducing oedema. The treatment has no effect on normal individuals. The cause of the oedema and the effect of treatment may be centred in the hypothalamus rather than the pituitary gland.

THE AETIOLOGY OF SENILE VULVO-VAGINAL PRURITUS AND ITS RATIONAL TREATMENT WITH FOLLICULIN.

The development of vaginal epithelium depends on ovarian function. At the menopause vaginal acidity is decreased to a *p*H of six or seven; this is due to atrophy of the basal layers of the mucosa and the consequent disappearance of glycogen. Secondary infection is therefore common. Hence, vulvo-vaginitis and functional pruritus due to atrophic changes should be treated with oestrin.

Fifteen cases of mild pruritus due to menopausal atrophy were all cured by injections of 0.1 to 1.0 milligramme of oestradiol benzoate. The good effect was apparent in 10 to 20 days, but when treatment was suspended a few cases relapsed.

Five patients who had severe pruritus of long duration required as much as 5.0 milligrammes of oestradiol benzoate weekly or twice weekly: this had to be continued for as long as eight weeks in some cases.

In severe pruritus complicated by leucoplakia or kraurosis 5.0 milligrammes were injected once or twice weekly for nine to 12 weeks; the results were not so good but in some patients the local lesions disappeared completely. This curative effect on leucoplakia has not been recorded by other workers.

The response is essentially an epithelial one, and for this reason oestrin may be of value in juvenile acne and senile skin changes. The administration of this hormone is contra-indicated in precancerous lesions.

This article is illustrated by macroscopic and microscopic photographs.

CLINICAL AND BIOLOGICAL CONSIDERATIONS REGARDING EXTRA-UTERINE GESTATION.

Although a negative Friedman test in a case of ectopic gestation allows the inference that chorionic activity has ceased, the author insists that operation should always be performed. For haematosalpinx, laparotomy is required, but only simple colpotomy is necessary when a pelvic haematocele has formed.

A case is described from which the following conclusions are drawn. (*a*) Before adopting a conservative attitude a negative biological test should be obtained. (*b*) The test may remain positive for as long as three weeks after death of the ovum. (*c*) If simple colpotomy is performed and the Fallopian tube left undisturbed the tubal lesion may heal so completely that no abnormality is revealed on salpingography.

If the amount of prolan in the blood-serum is less than 200 rabbit-units per litre surgical intervention may be delayed and further tests carried out to determine if the amount is decreasing.

The degree of danger of ectopic pregnancy and the need for urgent surgical treatment are proportional to the amount of prolan in circulation.

With regard to clinical features Bourg emphasizes the delay in development of physical signs and the persistence of bleeding after curettage.

Streptococcal Infection of Unknown Origin in a Woman Eigth Months Pregnant.

The patient previously had had six children and was admitted to hospital at the eighth month of pregnancy with symptoms and signs suggesting acute appendicitis. At operation the appendix was found to be normal but there was free pus in the peritoneal cavity, and adhesions round the right appendage.

The day after operation the patient developed bilateral broncho-pneumonia and labour commenced. The child presented by the breeeh and was stillborn. Streptococci were demonstrated in the maternal blood-stream and also in blood from the umbilical cord.

A few days later erysipelas of the abdominal wall developed, while on the twelfth day phlegmasia alba dolens made its appearance. Subsequently the patient had acute pyelitis and finally a metastatic abscess formed in the right of the lower abdomen and necessitated drainage.

After being in a precarious condition for some time, the patient ultimately recovered. The author suggests that the widespread infection had its origin in an acute exacerbation of a pre-existing chronic salpingitis. The virulence of the infection is borne out by the transmission of organisms through the placenta.

Rupture of Extra-uterine Gestation due to Folliculin.

In view of its action on the blood-vessels and muscle of the uterus, the author considers that oestrin can produce abortion in the human subject in the early months of gestation.

A case is recorded in which the diagnosis of salpingo-metritis was made. After conservative treatment has been carried out, 1,000 units of oestrin were administered with the object of bringing on menstruation which had ceased. Seven hours after the injection of the hormone the patient collapsed and presented the typical features of ruptured ectopic pregnancy. Immediately laparotomy was successfully performed.

Vanderzypen believes that the tubal rupture was directly due to the folliculin and considers that the administration of this hormone has the following dangers. (*a*) It produces abortion. (*b*) It may rupture tubal pregnancies. (*c*) It causes exacerbation of chronic inflammatory conditions.

Conversion of Mento-posterior Positions into Occipital Presentations.

Caesarean section is not the best treatment for all obstetrical difficulties, and the object of this paper is to emphasize obstetrical manœuvres which are in danger of being overlooked.

The diagnosis of face presentation can be made before the onset of labour or early in labour, but for this purpose the whole hand should be introduced into the vagina. No special treatment is necessary for anterior positions of the chin, but if the position is mento-posteeior then the following procedures are advised.

When the cervix is undilated, the membranes intact, and labour very little advanced, the manœuvre of Schetz is sufficient. By external manipulations the anterior shoulder is pushed upwards, the breech is then directed away from the foetal back, and finally the occiput is pressed over the pelvic inlet. The membranes may then be ruptured to ensure persistence of the new presentation.

If the membranes are ruptured, the foetal mortality limited, and the cervix two fingers dilated, both vaginal and abdominal manipulations are required: the latter are the more important. The anterior shoulder is raised and this is followed by upward pressure on the chin with the vaginal fingers. Finally, the occiput is pressed down into the inlet—Baudelocque's manœuvre.

The third class of case is that in which the patient has been long in labour, the cervix is fully dilated but the foetal head not engaged. Here the internal manœuvres are the more important. Having pushed up the anterior shoulder, a hand is passed into the uterus and round the occiput, pulling the latter down to present: external pressure is of assistance—Thorn's manœuvre

The author describes illustrative cases and finally mentions another method of treatment which is only of historical interest. This consists in passing one blade of the forceps behind the occiput and using it as a lever to promote flexion. Injury to the cervix is almost inevitable.

T. N. A. Jeffcoate.

Archiv für Gynäkologie.

Band 160, Heft 3, April 2nd, 1936.

The thyroid gland and pregnancy. A. Pohl.

Pituitary tumour and pregnancy. R. Reckmann.

The corpus luteum hormone (progesterone) and the genital tract in the male. E. Fels.

The de-aminizing function of the human placenta. J. Botella-Llusiá.

*Ovarian function many years after hysterectomy. H. Siegmund.

*The adrenal cortex and sexuality. H. O. Neumann.

The development of the germinal strands and the architecture of human germinal glands. P. Grünwald.

*Alterations in the mucous membrane (metaplasia) of the uterus from continued administration of follicular hormone. P. Grumbrecht.

*Ovarian hormone and ketonaemia M. M. Mendizábal, E. de Amilibia, and J. Botella-Llusiá.

Concerning an adenomyoma of the ovary R. E. Katzenstein.

The cholin and acetylcholin content of the immature human placenta. E. Strack and H. Geissendörfer.

Multinuclear ovum-cells, multiovular follicles and double follicles stained by vital methods. E. Strassmann.

*Degeneration and regeneration of vegetative nerve-tissue in the transplanted ovary. H. Goecke and J. Beaufays.

Statistical and experimental contributions to the question of factors influencing the relative proportions of the two sexes. III: Schoner's theory. A. Kaven.

Uterovenous reflux in hysterosalpingography. G. Effkemann.
*Thyroid treatment of habitual abortion. E. Werbatus.
Isohaemo-agglutination in assessment of paternity. S. C. Friemann.
Late sequelae of eclamptic diseases of pregnancy. H. Siedentopf and H. Major.

Band 161, April 6th, 1936.

In 430 pages and 70 papers this volume contains a full report of the proceedings of the twenty-fourth assembly of the German Gynaecological Society held at Münich from October 23rd to October 26th, 1935. The four subjects dealt with were: (1) Sterility. (2) The liver and pregnancy. (3) Climatic treatment, light treatment and hydrotherapeutic treatment. (4) The present state of experience in eugenic sterilization.

OVARIAN FUNCTION MANY YEARS AFTER HYSTERECTOMY.

In two rabbits, 24 to 30 months after hysterectomy, follicular ripening, ovulation and corpus luteum formation persisted in normal kind and degree; histological and other evidence is adduced that the absence of oestrus and the absence of ovulation after coitus in these animals, when they have been kept in isolation from the males, is not due to persisting corpus luteum activity but probably to defective pituitary function. In the healthy human subject after hysterectomy periodic mammary signs, occurring through many years, afford evidence of cyclical ovarian activity. The healthy female can compensate for the loss of the uterus without experiencing menopausal symptoms: when the reverse appears to be true ovarian malfunction preceded operation or was caused by operative trauma. Nevertheless, in surgery preservation of the uterus or a part of it, as in myomectomy, is laudable on psychic and other grounds.

THE ADRENAL CORTEX AND SEXUALITY.

Deficiency in the adrenal cortex, as in Addison's disease, diminishes sexual function and in the female causes atrophy in the ovary and finally amenorrhoea. A patient having symptoms of Addison's disease had oligomenorrhoea and endometrial atrophy: regular menses returned, as cutaneous pigmentation regressed, with treatment by cortical hormone and vitamin C. Excessive adrenal cortical activity (as in tumour cases) often causes in children precocious puberty; in sexually mature women masculinization (virilism or "inter-renalism"); and in males (quite rarely) a reversal of sex-characters—provided sexual maturity has not been attained. In one of three cases of hypernephroid blastoma here described, well-marked virilism disappeared after removal of the tumour and a living child was subsequently born. Three further cases are described of hypernephroid blastoma of the female genital organs: in one the urine gave a positive Grade III Zondek-Aschheim test, which became reduced to Grade I after operation. The conclusion is stated to be probable that the cortical hormone in affecting the genital sphere acts primarily by influencing the hypophysis.

ALTERATIONS IN THE MUCOUS MEMBRANE (METAPLASIA) OF THE UTERUS FROM CONTINUED ADMINISTRATION OF FOLLICULAR HORMONE.

Grumbrecht found that in white rats, whether castrated or not, long continued injections of high doses, e.g. 6,000 mouse-units, equivalent to

30,000 international units, of progynon B. oleosum, i.e. the benzoic ester of dihydrofolliculin, daily for 60 days, caused in many cases the cylindrical-cell endometrium to be replaced by squamous epithelium of many layers, the superficial zones showing keratinization. Penetration of the myometrium by finger-like ingrowths of the epithelium was noted, but the basal membrane, though invaginated, was respected and true infiltration as by tumour was not found. Cell nests were present. Eosinophile infiltration of the stroma of the mucosa was very well marked. The uterus was greatly enlarged and congested and in some cases the hyperplastic endometrium had been cast off. The blood of the test animals was free from any antibody to follicular hormone.

Ovarian Hormone and Ketonaemia.

In rabbits and in rats injections of follicular hormone, from six hours to six days, increase the blood-content of ketone bodies, and injections of luteal hormone have the opposite effect. Both results are to be connected firstly with hepatic metabolism, for folliculin diminishes the hepatic glycogen and lutein increases it, and, secondly, with thyroid function, for the ketonaemic alterations are absent in animals injected with folliculin and lutein after having been subjected to thyroidectomy.

Degeneration and Regeneration of Vegetative Nerve-tissue in the Transplanted Ovary.

In a previous work Goecke has found that the bud-like or sling-like terminals which have been described in nerve-fibrils in the ovary are either artefacts or errors of interpretation: he states that the fibrillary terminations envelope the cells like a veil and in places actually penetrate them. Such a finding would suggest that the ovary is subjected to autonomic nerve control to a much greater extent than is commonly supposed. As might be expected degenerative processes are found both in the nerve-fibres and their terminal reticula in experimental ovarian transplants. Goecke and Beaufays now report that so early as the ninth day nerve regeneration, arising from the surrounding tissues, is to be found. Vegetative nerve-tissue from these penetrates the transplant along the course of the ingrowing vessels.

Thyroid Treatment of Habitual Abortion.

Previous reports of successes of this treatment are mentioned, together with Sellheim's favourable results from administration of serum from healthy pregnant subjects. Werbatus describes 23 cases in which from two to six abortions had occurred with negative Wassermann reaction. All but one went to term in a pregnancy during which three tablets of 0.1 gm. had been given daily until quickening, then three of 0.2 gm. until the eighth month and three of 0.3 gm. until the onset of labour. No inconvenient effects were observed.

Late Sequelae of Eclamptic Diseases of Pregnancy.

This paper contains a record of systematic examination, during a short stay in hospital, of 29 patients who had had severe pregnancy nephropathy

or eclampsia from two to eight years previously. (It is suggested that in the past attention in these investigations has been too closely focused on the kidneys). In the 13 nephropathics the non-protein nitrogen was invariably normal, but seven had increased blood-urea and five had an increase of xantho-protein. Ten had subjective cardiopathic symptoms and four showed oedema, four silver-wire arteries in the fundus oculi, five hyperpiesis, and six morbid objective signs in the heart. Of the 16 former eclamptics half had albuminuria, nine an increase of blood-urea, and 13 morbid cardiovascular signs and symptoms.

W. E. Crowther.

Zentralblatt für Gynäkologie.

No. 38, September 19th, 1936.

*The development of operations for vesico-vaginal fistulae. W. Stoeckel.
Abscesses of Skene's glands. W. Lindemann.
Diverticulum of the urethra with a concretion. K. Podleschka.

No. 39, September 26th, 1936.

Chemotherapy and prophylaxis of streptococcal infections by means of alkaline bile acids. R. Hilgermann.
A soft skull as the object of obstetrics. R. Cordua.
Pulmonary tuberculosis and gynaecological operations. H. Dietel.
Inguinal lymphogranuloma. R. Peter.
*Vesicular mole in a woman 55 years of age. H. Feenders.
An investigation of potassium metabolism in healthy pregnancy and in toxic pregnancy. F. Szüsz.

No. 40, October 3rd, 1936.

*The prospects of the treatment of sterility and their political value. G. K. F. Schultze.
*Results of treatment of sterility. Kl. Gerloff.
Living or stillbirth. Fr. Kirstein.
The stimulation of male sex glands by female sex hormones. W. Pettersson.
*The inhibitory action of follicular hormone upon milk secretion in the puerperium. J. M. Mayor.
Vinethen in obstetrics. H. Richter.

No. 41, October 10th, 1936.

Domiciliary midwifery and abdominal section. F. Siegert.
The management of the third stage of labour in Caesarean section. K. de Snoo.
*Giant mixed tumour of the uterus. H. Rockstroh.
The treatment of asphyxia neonatorum with coramin. W. Nagel.
The treatment of pruritus vulvae with progynon. M. Rodecurt.
*The experimental production of corpora lutea in the ovaries of rabbits. V. S. Kaandaratsky.

No. 42, October 17th, 1936.

*Studies of transportation of the ovum in women. P. Caffier.
Legal sterilization in the puerperium. E. Puppel.
Short-wave colpeurisis. G. Zimmer.
Galea forceps in obstetrics. G. v. Pall.
The therapy of cervical fluor. M. Rodecurt.

No. 43, October 24th, 1936.

Vesical endometriosis. F. v. Mikulicz-Radecki.
Vesical foreign bodies in the female. M. M. Korezky.
Bilateral renal calculi during pregnancy. H. Schwalm.
Anuria during labour and the early puerperium. E. Steinkamm.
*Bilateral absence of the kidneys in the newborn. A. Vetter.
*Cystic kidneys and their operative treatment in the newborn. Chr. Jensen.

No. 44, October 31st, 1936.

Osteitis fibrosa and osteopsathyrosis in a contracted pelvis. P. Esch.
The X-ray diagnosis of submucous myomata. R. Prevot and W. Schultz.
The hormonal diagnosis of pregnancy. Hj. Wespi.
*Follicular hormone in hyperthyroidism. Vr. Jonas and E. Markalous.
Remarks on some newer works upon the trichomonas as a cause of leucorrhoea and a plea for a definite treatment of trichomonas. M. Rodecurt.
Late results of artificial vaginal plastic operations. W. G. Wargassowa.

No. 45, November 7th, 1936.

*Clinical and hormonal mistaken diagnosis of extra-uterine pregnancy in the case of a cyst of the corpus luteum. K. Ehrhardt and H. Kramann.
The chemical diagnosis of pregnancy from the urine. E. Scipiades, junr.
Kraurosis fornicis vaginae. J. Novak.
A new safe method for the avoidance of retention of swabs after laparotomy. H. Schwanen.
Spontaneous delivery in the presence of a gigantic myoma. H. Kraatz.
Experimental adenomyosis of the uterine cavity after the injection of tincture of iodine into the rabbit. W. Zaleski.

No. 46, November 14th, 1936.

The hormonal place of the decidua. E. Philipp and H. Huber.
A clinical statistical investigation into the occurrence of uterine hypoplasia as a late result of war diet. E. Wehefritz and E. Gierhake.
The operative treatment of tubal sterility. B. Tritschkoff.
Diagnositic aids in interrupted ectopic pregnancy, with especial reference to pyramidon investigation. G. Tsutsulopulos.
Rupture of the aorta in septic abortion. F. Hellner.
*The technique of Caesarean section for placenta praevia. H. Högler.

THE DEVELOPMENT OF OPERATIONS FOR VESICO-VAGINAL FISTULAE.

Stoeckel read a paper at the celebration of the sixtieth anniversary of the Berlin Obstetrical and Gynaecological Society. He chose as his subject a review of all the different methods which have been used in the operative

treatment of vesico-vaginal fistula. He pointed out that there was a considerable degree of muddled thought on the subject of the method of healing of these fistulae, and for this reason he drew up a classified list of the different methods and afterwards gave a detailed illustrated description of the different procedures. His table was as follows:

1. Methods of direct closure of vaginal fistula. (*a*) Plastic operations after Simon; extirpation of the fistulous canal. (*b*) Dedoublement, division of the fistulous canal. (*c*) Complete mobilization of the bladder; elimination of the fistulous canal. (*d*) The cuff method; tissue tamponage of the canal.

2. Plastic flap operations. (*a*) With one flap. (*b*) With two flaps.

3. Under-padding methods. A. Implantation methods: (*a*) Metroplastic operations after Küstner. (*b*) Corpus implantation after W. A. Freund. (*c*) Fundus implantation after Scheckele. (*d*) Portio implantation after McLean. (*e*) Colpocystoplastic operations after Witzel. (*f*) Autocystoplastic operations after Witzel. B. Interposition methods: (*a*) Interposition of the uterus after Wertheim-Schauta. (*b*) Interposition of the vesical wall after L. Fränkel. (*c*) Interposition of the peritoneum. (*d*) Interposition of free transplanted fascia.

4. Abdominal operative methods. (*a*) Method of Trendelenburg; extraperitoneal and intravesical. (*b*) Method of L. Seitz; intraperitoneal and intravesical. (*c*) Method of v. Dittel; intraperitoneal and extravesical. (*d*) Method of Bardenheuer; extraperitoneal and extravesical.

5. Vaginal approach to the fistula by means of incisions. (Duhrssen, Schuchardt, Samter.)

6. Ventral vaginal methods. (Fritsch, Schauta.)

7. Methods when the urethra is involved. (*a*) Reconstruction of the sphincter vesicae. (*b*) Substitution and support of the sphincter. (i) Pyramidalis fascial ring (Goebel, Frankenheim, Stoeckel). (ii) Levetor plastic operation. (iii) Double-sided levator hold. (iv) Bulbo-cavernosus plastic operation. (*c*) New formation of the urethra.

8. The insurance of reproduction of normal conditions. (*a*) Kleisis methods. (*b*) Implantation of the ureters into the colon.

9. Repeated fistula operations.

10. Methods employing caustics.

11. Preparation and after treatment.

12. Choice of method and combination of methods.

A detailed consideration of the various methods employed was further clarified by 30 most excellent illustrations, semidiagrammatic in type.

While he does not lean towards any one method of treatment Stoeckel pointed out that all the different methods or their combination had been successful in the hands of different operators.

Vesicular Mole in a Woman 55 Years of Age.

Feenders, of Danzig, records the case of a woman, 55 years of age, who became pregnant after having had six full-time deliveries and four miscarriages. Her last delivery had been complicated by a placenta praevia in 1926. Her last menstrual period occurred in July 1935.

On January 10th, 1936, she complained of prolonged uterine bleeding, the uterus being enlarged and the adnexa not palpable. The condition was diagnosed as being one of climacteric bleeding, and she was treated with

ergot without improvement for three weeks. On February 1st the uterus was curetted and the specimen recovered sent for pathological examination.

Sections showed the material to be placental in character with free bleeding into the decidua and numerous chorionic villi which had undergone a degeneration typical of vesicular mole. There was overgrowth of chorionic epithelium but no definite evidence of chorion-epithelioma.

The patient was kept under observation, and after some weeks the Aschheim-Zondek reaction was found to be strongly positive. In view of this and the known chorionic overgrowth the patient was suspected to be suffering from chorion-epithelioma which had been missed by the curette. On March 25th the uterus and adnexa were completely extirpated.

Examination of the specimen showed a fairly well-involuted uterus with a mucosa poor in glandular elements. In the mucous stroma there was a free deposit of haemosiderin, and at one spot there were some poorly shown decidual cells and some wandering chorionic cells, with neighbouring bleeding. In the neighbourhood of the left tubal angle there was a circumscribed haematoma in the muscularis in which some further necrotic chorionic wandering cells were found. Sections cut from different parts of the uterus failed to show any evidence of malignant change.

While recognizing the possibility of a positive Aschheim-Zondek reaction with retained portions of chorionic tissue which have not undergone malignant change the writer considers that the radical operation was justified under the suspicion of a missed chorion-epithelioma.

THE PROSPECTS OF THE TREATMENT OF STERILITY AND THEIR POLITICAL VALUE.

Schultze describes fully the practice of a sterility clinic which has been in operation since 1927 in Berlin, dealing in the nine years of its existence with nearly 1,000 cases. In his cases the percentage incidence at different ages was 11 per cent 20 to 25 years, 39 per cent 26 to 30 years, 34 per cent 31 to 35 years, 14 per cent 36 to 40 years, and 2 per cent 41 to 64 years. The duration of sterility varied from one to 20 years, 56 per cent of all cases having lasted one to five years. Of his total 952 cases 53 per cent were cases of primary sterility and 47 per cent of secondary sterility. Of the cases of secondary sterility 10 per cent were post-partum, one per cent extra-uterine pregnancy, and 36 per cent post-abortum, showing that sterility following abortion was far the greatest factor in secondary cases.

All cases were investigated after a comprehensive routine, whether the cause of the sterility was obvious at the outset or not. A bimanual examination under a general anaesthetic was followed by an investigation of uterine secretion including the menstrual behaviour. X-ray examination after the injection of lipiodol as well as microscopy of the seminal fluid was undertaken for all cases. As a result female sterility was grouped under four heads: (1) Uterine sterility. (2) Sterility from genital underdevelopment. (3) Tubal sterility. (4) A small remainder described as constitutional sterility.

The uterine sterility group included such conditions as uterine displacements, myomata, cervical glandular changes, and endometrial changes. The treatment of this group gave satisfactory results in from 40 to 60 per cent. The hypoplastic cases after treatment with hormones varied con-

siderably from year to year, but averaged a satisfactory result in about 30 per cent of cases.

The results of treatment of sterility from double closure of the Fallopian tubes were extraordinarily bad. Of 320 cases only 13 became pregnant, 140 were treated conservatively with no result, and the 13 cases in which treatment was successful followed operative interference, namely only seven per cent. The cases of so-called constitutional sterility occurred in marriages where no abnormality was found in either man or wife. Advice as regards diet, climate and sexual hygiene resulted in conception in only 10 per cent of cases. Taking his cases as a whole the writer found that he obtained a successful result in only 20 per cent.

Considering the number of marriages in Germany to be about 500,000 to 600,000 yearly and the percentage of sterile marriages to be 19 per cent, the writer points out that the loss in population, even if each marriage produces only two children, would be somewhere about 200,000 children yearly. If a determined effort were made to investigate and treat all sterile marriages in the country, and the results were only half as good as those of the Berlin clinic, yet 10 per cent of satisfactory results would produce a yearly increase of 20,000 children. The writer considers that even such a small percentage would be well worth while as a national effort to increase the population of the country.

THE RESULTS OF THE TREATMENT OF STERILITY.

Gerloff refers to cases treated for sterility in the clinic at Königsberg during the two years July 1st, 1933, to June 30th, 1935. During this period 102 cases of female sterility were investigated and classification was found to fall under the same four heads as Schultze found in Berlin. His results were very similar to those of Schultze allowing for the smaller number treated. Out of 102 cases treated 16 patients became pregnant, and of these 11 have been delivered of living children and five are now normally pregnant.

THE INHIBITORY ACTION OF FOLLICULAR HORMONE UPON MILK SECRETION IN THE PUERPERIUM.

Mayor describes his investigation of the results of treatment of 47 women in the clinic at Königsberg who had been recently delivered and in whom lactation was not to be established. The cases included deliveries at term, premature deliveries and abortion. A hormonal injection was made during the first 24 hours after delivery and then once daily, the injection being intramuscular in each case: 14 cases were given menformon and the rest progynon B. oleosum.

The following results were obtained as a result of this investigation: (1) The intramuscular injection of follicular hormone undoubtedly had an inhibitory effect on mammary secretion. (2) Daily doses of 200 to 10,000 mouse-units of follicular hormone six to eight days after each other produce no clinically valuable result. (3) Doses of 250,000 mouse-units of follicular hormone in one injection produce a valuable clinical result. (4) The exact boundaries of the indications for such treatment will have to be worked out after experience on further cases has been obtained. The writer would suggest its use in all cases with a dead foetus or an abortion.

GIANT MIXED TUMOUR OF THE UTERUS.

Rockstroh describes the case of a patient, aged 59 years, who had had four children: she reached the menopause at 53 years. She noticed that her abdomen had increased in size during the previous year, and for three months she had suffered from a bearing-down sensation followed by pressure symptoms for five weeks. She was found to have a large uterine tumour which filled the pelvis and reached to within a hand's breadth of the sternum. The uterus was removed and was found to weigh 6.5 kilograms and to measure 26 by 22 by 22 centimetres.

Operation was followed by an uninterrupted recovery. The tumour was found to be an interstitial lipomyoma of the uterus. The muscular wall of the uterus was atrophic as a result of the pressure of the expanding fatty tissue and large cell growth which appeared to have been derived from muscle cells.

Illustrations are given to show the microscopic appearance both of the tumour and of the atrophic muscular wall with large cell growth.

EXPERIMENTAL PRODUCTION OF CORPORA LUTEA IN THE OVARIES OF RABBITS.

Kandaratsky, working with a series of rabbits in different stages of follicular development at the Experimental Institute at Kasan, came to the following conclusions.

1. Artificial rupture of the follicle and the consequent trauma has no influence on the later physiological processes.

2. After artificial rupture of the follicle in the rabbit, whose ovary is in a resting stage, is not followed by the production of the corpus luteum. The follicle collapses with the subsequent formation of a corpus albicans.

3. Follicular rupture not later than 10 hours after fertile or sterile coitus will be followed by the development of the corpus luteum.

4. These changes into corpora lutea occur only in follicles which have reached an advanced stage of maturity.

5. Follicular rupture with subsequent treatment with prolan was always followed by development of the corpus luteum. This result occurred whether the rupture was artificial or physiological.

6. The conversion of the follicle into a corpus luteum in the majority of cases under the influence of prolan is not preceded by rupture. Although in general the development of the corpus luteum follows rupture of the follicle, this is by no means an essential precursor.

7. Under the influence of prolan following artificial follicular rupture and the development of a large number of corpora lutea the process of follicular ripening in the ovary is hastened.

8. The cells of a corpus luteum produced by the action of prolan contain a large proportion of lecithin and a small amount of neutral fat.

9. During the changes into the corpus luteum the cells of the *cumulus proligerus* retain their normal structure while the granulosa cells of the follicular wall in other parts degenerate.

10. The formation of the corpus luteum in the rabbit must be looked upon as a progressive process.

11. The presence of the ovum whether after spontaneous rupture or artificial removal has no influence upon the change from the follicle to the corpus luteum.

12. The retained ovum in a corpus luteum is deficient in hyalin.

STUDIES IN THE TRANSPORTATION OF THE OVUM IN WOMEN. SECOND COMMUNICATION. THE QUESTION OF EXTERNAL MIGRATION OF THE OVUM.

Caffier, after further investigation into the question of the movements of the ovum, comes to the following conclusion. It has been observed that if an injection of prolan is made before the expected ovulation, the fimbriae of the Fallopian tube which does not belong to the ovulating ovary also take part in the transportation of the ovum. It does not follow that external migration of the ovum only occurs when the pregnancy is found in the Fallopian tube on the opposite side to that of the corpus luteum. It may well be that an intra-uterine pregnancy may have reached its destination after the ovum has been propelled into the open abdominal end of the opposite tube. If this supposition is correct it would seem important to retain a tube on the side from which an ovary has been removed with a view to increasing the possibility of tubal function.

BILATERAL ABSENCE OF THE KIDNEYS IN THE NEWBORN.

Vetter records the case of a male foetus born prematurely and living. The membranes ruptured after the presenting breech was distending the pelvic floor and there was no escape of liquor amnii at any time during the labour. The foetus weighed 2,250 grams and measured 44 centimetres, it was apparently normal at birth. Two and a half hours after birth it suddenly became cyanotic and died. At the post-mortem examination the foetus externally had the appearance of a normal male with the caput on the scrotum. On opening the abdomen there was complete absence of both kidneys, ureters, bladder and renal vessels. The suprarenal glands and genital structures were normal; the urethra ended blindly 1.5 centimetres from its external orifice.

The writer points out that this abnormality is very rare apart from gross foetal deformity. He has been able to trace only 10 other cases of absence of both kidneys in an otherwise normal foetus, and in these recorded cases no cause for the renal failure has been ascertained, such factors would have to come into operation at the fourth week of pregnancy. In all 10 cases there was complete absence of liquor amnii though this condition was not recognized until after labour had begun.

It would appear that the renal function is not essential for intra-uterine life although death took place shortly after birth.

CYSTIC KIDNEY AND ITS OPERATIVE TREATMENT IN THE NEWBORN.

Jensen records the birth of a full-time female foetus which was the second child of a normal woman. Delivery ran a normal course until after the birth of the head and then extraordinary difficulty was experienced in extracting the shoulders and trunk. The foetus was born alive, measured 56 centimetres, and had an abdominal circumference of 43 centimetres. Palpation of the abdomen showed an elastic tumour the size of a foetal head which filled the whole left half of the cavity and extended over the middle line to the right side. There was no ascites and the foetus otherwise appeared normal. X-ray investigation and a normal blood-count decided the diagnosis of a retroperitoneal tumour probably of renal origin.

As the circumference of the abdomen increased to 45 centimetres in the eight days after birth, an attempt at removal was decided on, and this was

carried out through a left lumbar incision under ether anaesthesia. The baby stood the operation well and left the hospital well. The specimen consisted of the left kidney transformed into seven or eight cysts, the whole tumour being of the size of a foetal head and weighing 840 grams. There was no sign of any malignant change.

The later observation of the baby up to 22 months found its development to be absolutely normal without any sign of renal insufficiency.

STUDIES OF FOLLICULAR HORMONE IN HYPERTHYROIDISM.

Jonas and Markalous from an investigaion of cases of hyperthyroidism in Prag have come to the following conclusions. Women with hyperthyroidism have a definitely low urinary follicular hormone content in comparison with normal women, and also in comparison with other ill women whose menstrual cycle is normal. Furthermore, those suffering from oligomenorrhoea and amenorrhoea during the course of their illness have a less urinary follicular hormone content than those who are examined during a period of remission of their illness.

In two cases in which repeated examinations were carried out during the course of the illness one showed no change in the follicular content at the height of the illness, while the other had an increase as the condition improved.

MISTAKEN DIAGNOSIS OF EXTRA-UTERINE PREGNANCY ON CLINICAL AND HORMONAL GROUNDS.

Ehrhardt and Kramann describe the case of an unmarried woman of 30 years of age who suffered from bearing-down pains and one month of amenorrhoea. She considered herself to be pregnant, and on pelvic examination this was thought to be correct but that the pregnancy was extra-uterine, because there was a cystic swelling as large as an apple in the right fornix and some uterine enlargement. The swelling increased slightly in size during the five days the patient was under observation, and the Aschheim-Zondek reaction was positive.

The abdomen was opened under the belief that the case was one of extra-uterine pregnancy, but no pregnancy was found. The right ovary was cystic and enlarged; it was removed. Histological examination of the specimen showed it to be an ovary containing a cyst of the corpus luteum. Further urinary examination one day and eight days after operation gave positive reactions on the first occasion, and a positive reaction A and a negative B on the second occasion. In view of these findings in this patient a second patient of 20 years with similar symptoms and physical findings who denied the possibility of pregnancy was treated on expectant lines with ultimately satisfactory results. In this case reaction A remained positive for six days and reaction B remained positive for two days. After 10 days the patient was discharged well without operation. The occurrence of a positive Aschheim-Zondek reaction in the presence of a persistent corpus luteum renders this reaction of less value in the diagnosis of suspected tubal pregnancy and should be kept in mind in dealing with an early case.

THE TECHNIQUE OF CAESAREAN SECTION IN PLACENTA PRAEVIA.

Högler refers to the well-known fact that a uterus containing a placenta praevia which is partially separated will bleed from the detached placental

site so long as the placenta remains in the uterus. If the placenta is completely detached and removed the bleeding will stop even if the foetus is not yet delivered.

Under these conditions the chief haemostatic factor cannot be that of muscular retraction because this is prevented by the presence of the foetus in the uterus. He considers that arrest of bleeding in this case follows a process of vascular retraction at the placental site.

Under this supposition the writer has in some cases of Caesarean section for placenta praevia, separated the placenta and removed it before extracting the foetus. He has used this method of delivery when the bleeding has been very free and the condition of the foetus has allowed of a few minutes delay in its delivery.

When the placenta has been removed before the extraction of the foetus the writer has noticed that there has been a prompt cessation of the bleeding, and for this reason he recommends its adoption when delivery by Caesarean section is carried out for placenta praevia with free bleeding.

R. H. B. Adamson.

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*Temporary sterilization of women *per vaginam*. A. J. Krupsky.

*Rare indications for interrupting pregnancy. O. Eisenreich.

An interesting disturbance of the circulation in the umbilical cord as a rare cause of abortion. A. Ebergenyi.

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*Experiences with the interposition operation of Schauta-Wertheim. J. Frei.

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*Cerebral pressure in eclampsia and its relation to the onset of fits. G. Spoljanskij and A. Juzelrvskij.
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*An apparent potentiation by combining oxytocic drugs. K. Schubel.
The value of galvanic sensitivity for the recognition of eclampsia. R. Spiegler.
*The value of pyramidon tests in extra-uterine pregnancy. A. S. Bychowskaja.
*Investigations with carp as a method of diagnosing pregnancy. F. Szusz.
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A prophylactic correction by plastic operations of bicornute uteri. F. Rhemann.
*Two cases of puerperal infection by a gas-forming bacillus. G. Simonsitz.
*The significance of general disturbance in pregnancy and labour as a predisposing factor for eclampsia. J. Fressel.
The magnesium content of the serum. R. Spiegler and E. Naumes.
*Investigations of the gastric acidity in women with genital cancer. K. Fuge.
The rational treatment of mastitis and mammary fistula with diathermy. A. N. Poljanskaja.
Intra-uterine injury to the foetus. W. T. Schmidt.
A satisfactory case of ileum substitution for vaginal atresia. W. T. Schmidt.

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The cause of congenital skin and periosteal defects of the cranium. H. E. Scheyer.
*Schloffer's tumours. L. L. Horn.
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The potassium and calcium content in the blood of the newborn in relation to the menstrual cycle. A. Schepetinsky.
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*Weltmann's coagulation band in pelvic infection. F. G. Purper.
*The action of anterior pituitary hormone on non-functioning ovaries. R. A. Tschertok and G. W. Penkow.
A full-time interstitial pregnancy. H. Tietze.
The results of treating vaginitis and erosions during pregnancy. N. A. Borissowa.

TEMPORARY STERILIZATION OF THE WOMAN *per vaginam*.

The author describes a method of temporary sterilization which he has devised, whereby he occludes the cervical os and makes a new opening higher up in front of the cervix.

He carried out the operation 11 times in patients between 25 and 35 years of age. In two cases the cervical os failed to close and one patient subsequently became pregnant. In one of the remaining nine patients four and a half years have elapsed since the operation, and in another eight years have elapsed. The general health of all the women is good. Menstruation is proceeding as previously, being normal and painless. It has not yet become necessary to open the occluded cervix.

RARE INDICATIONS FOR INTERRUPTING PREGNANCY.

From a review of the literature the author shows that there is no doubt that pregnancy stimulates growth and recurrence in cases of malignant disease. There is also evidence that cancer will retrogress occasionally after evacuation of the uterus. He therefore argues that it is justifiable to terminate pregnancy in patients who are suffering from malignant disease. In conclusion, he describes the history of a patient who gave birth to successive children suffering from abnormal development, and gives this as a eugenic indication for sterilization.

THE NORMAL POSITION OF THE FOETAL HEAD *in utero*.

The author examined by means of X-rays a series of 80 pregnant women with a view to ascertaining which parts of the head were touched by the palpating hands in the fourth grip. In all the cases the child was in the anterior position. A special metal instrument was secured in position and the radiograms taken. It was found that the normal position of the foetal head was partly flexed, even before fixation. The brow was on an average two fingers'-breadth higher than the occiput, and these findings were true for primigravidae as well as multiparae. In the fourth grip the fingers usually touch the glabella, frontal bone or orbital ridges.

RENAL APLASIA WITH ABNORMAL DEVELOPMENT OF THE UTERUS.

The author describes two cases with renal aplasia. In the first there was a uterus pseudo-didelphys, i.e. a uterus duplex with a solid right horn, vagina and haemato cervix (there was aplasia of the right ovary). In the second there was a uterus bicornis septus, a septate vagina with a myoma in the left horn and aplasia of the left kidney.

The first patient suffered from mechanical dysmenorrhoea. The second patient was delivered of a full-time child after pregnancy in the non-myomatous horn.

THE PRESENCE OF A GROWTH-STIMULATING SUBSTANCE IN THE MENSTRUAL FLUID.

The author carried out a series of investigations on plants to discover the effect of menstrual blood on them. He proved that there was both a growth-stimulating and a growth-retarding substance present. The addition of blood to plants in test tubes stopped their growth, but if the plants

were grown in the earth growth increased. The author therefore points out that the varying results described in the literature are probably due to the method of experiment. There is no foundation for the surmise that menstrual blood contains either a specific poison, or a growth hormone. The results produced are probably due to its manurial effects.

EXPERIENCES WITH THE INTERPOSITION OPERATION OF SCHAUTA-WERTHEIM.

The author carried out 242 operations interposing the uterus between the bladder and the vagina. He believes that this is a good operation for prolapse of the uterus and vagina. It is specially useful for large cystoceles with minor degrees of prolapse. He does not recommend it for complete procedentia. During the child-bearing period it is essential to produce sterilization by ligaturing the Fallopian tubes. In his series of 242 interposition operations he had no mortality.

He therefore concludes that the operation has more use than any of the other reparative operations. The primary healing is always good and the late results singularly free from recurrence.

ABORTION AND STERILITY.

The author investigated 200 patients who had had abortions, and classifies them according to age, parity, etc.: he found that after abortion 18 of the women remained sterile for over two years, 36 for three years, 24 for four years, 82 for five to 10 years, 34 for 11 to 15 years, and six for 15 years: 86 per cent of the women were under 35 years of age. He classifies the supposed causes for the sterility and gives tables.

CEREBRAL PRESSURE IN ECLAMPSIA AND ITS RELATION TO THE ONSET OF FITS.

The authors investigated the cerebral pressure manometrically in cases of eclampsia and found that it varies between normal limits. The normal pressure in the cisterna magna was 150 millimetres of water in the supine position and fell to *nil* when the patient sat up. An increasing lumbar pressure was not always associated with an increase in the cerebral pressure. Antecedent anaesthesia with chloroform produces no drop in the pressure. The pressure in the subarachnoid region drops when liquor is removed no matter in which region the puncture is made. The authors found no support for the statement that an increased cerebral tension was responsible for the onset of fits.

IMPLANTATION ENDOMETRIOSIS.

The author points out that in the last few years a number of cases of endometrioma developing in operation scars has been described and gives details of another case in which pregnancy was terminated by abdominal section as sterilization had to be carried out. Endometriosis must have been transferred to the abdominal wall during the operation as an endometrioma developed there.

AN APPARENT POTENTIATION BY COMBINING OXYCYTOCIC DRUGS.

The author points out that for a number of years now it has been known that a combination of quinine and pituitrin produces a better effect than when each is used separately.

THE VALUE OF PYRAMIDON TESTS IN EXTRA-UTERINE PREGNANCY.

The author showed that pyramidon was not specific. It demonstrated the presence of derivatives of the red-blood corpuscles and is of value for substantiating the presence of intraperitoneal haemorrhage.

A negative test does not exclude the presence of a disturbed extra-uterine pregnancy. The haematin reaction is absent during menstruation.

A positive haematin reaction in malignant disease points to inoperability and that there is haemorrhagic ascites.

In cases of inflammatory exudate a positive test suggests haemorrhage. The test is positive in blood infections such as septicaemia and malaria. The technique of the test is described. The blood must be carefully obtained to be of value for testing as haemolysis mitigates against correct results.

In conclusion, the author states that the test has very little diagnostic value.

INVESTIGATIONS WITH CARP AS A METHOD OF DIAGNOSING PREGNANCY.

The author utilized carp (*rhodeus amarus*) from five to eight centimetres long in which, between April and June, a laying tube develops which is a little longer than 20 millimetres. This is reduced to one or two millimetres in length, after the eggs have been deposited.

Fleischmann and Kahn have demonstrated that this increase in size is due to the action of a hormone. Ehrhardt and Kuhn first utilized these experimentally to differentiate between pregnancy and non-pregnant urine by adding the urine to the water in the aquarium.

The authors carried out experiments with 259 fish. Between May and August the laying tubes were between two and four millimetres long. The fish were kept in six litre jars, three being placed in each container, air being continually bubbled through. The fish were fed with daphnia. They also added from five to 10 cubic centimetres of urine per litre of water. The authors experimented with boiled and normal pregnant urine, non-pregnant and male urine, ovarian hormone preparations, and anterior pituitary preparations: 32 fish were kept in pure water as controls.

The results of the experiments were that it was only possible to produce a change in the laying tube during the heat period and it was not possible to make the diagnosis more rapidly.

TWO CASES OF PUERPERAL INFECTION BY A GAS-FORMING BACILLUS.

The author states that there is a form of local gas bacillus infection without special clinical symptoms which can only be discovered by bacteriological examination. They show slight rises of temperature and even rigors without producing typical blood changes.

In other cases the blood becomes infected with the bacillus phlegmonis emphysematosa. Roma found 20 cases among 171, Lehrmann 18 among 100 cases of bacteraemia.

The author gives abstracts from the literature describing the symptoms of typical cases of gas bacillus infection and gives in detail the history of several cases of his own. One case was cured, and this is ascribed to the timely application of an appropriate antiserum.

THE SIGNIFICANCE OF GENERAL DISTURBANCE IN PREGNANCY AND LABOUR AS A PREDISPOSING FACTOR IN ECLAMPSIA.

The increase in weight during pregnancy should be taken into consideration with increase in the blood-volume. Investigations showed that an average of three to five kilogrammes should be allowed for the foetus and liquor amnii. There was an increase of 0.6 per cent of the body-weight. The uterus itself increased 20 times in weight. In order to provide for the nutrition, metabolism and growth of the foetus, Hansen estimated the blood-content of the uterus to be one litre: the transverse section of the uterine arteries was found to be double. This increased the flow of blood through the uterus.

The author points out how this large blood collection can have an influence on all the organs of the body, and if slight disturbance of the circulation ensues, especially the sponge-like liver and the kidneys, they should receive twice their weight in blood every minute and 10,000 litres in 24 hours.

The author pointed out how the venous pressure is raised when the uterus contracts with an effect on the plexus in the true pelvis influencing the blood in the inferior vena cava.

At the same time the increase of the intra-abdominal pressure brought about by respiration has a marked effect. This interferes with the emptying of the veins and hinders the heart.

There is an increase in the size of the portal vein with overfilling of the liver. The lymphatic vessels are also over-filled with increased pressure in the thoracic duct and hyperaemia of the area drained by the superior vena cava. The whole of the corporeal musculature is thus influenced. In this way changes are brought about in the brain and other foetal organs.

The author draws attention to experimental and other clinical conditions in which stress on the venous system brings about renal changes.

INVESTIGATIONS OF THE GASTRIC ACIDITY IN WOMEN WITH GENITAL CANCER.

The author investigated the gastric acidity in 80 women with uterine carcinoma. In 15 there was a deficiency of acidity and in 25 there was normal acidity. They were mostly inoperable cases which had been sent for radium therapy. A simultaneous haematological investigation showed that there was anaemia.

He found that quite severe pains could be brought about by hypo-acidity and could be relieved by the following prescription: Acid hydrochlor. non-dil., 20 parts; pepsin sic., 20 parts; Aq. dist., 200 parts; sig. 3 t.d.s.

SCHLOFFER'S TUMOURS.

Schloffer in 1908 described five cases of tumours in the abdominal wall. Usually silk thread was found in the middle of the swelling and staphylococcus aureus or albeus could be grown from the abscess. The conclusion was that these organisms were introduced with the suture material. Other cases in the literature are referred to, but evidence of malignancy was never found.

The author gives the details of a case. The tumour was adherent. The differential diagnosis was actinomycosis, desmoid tumours, sarcoma, and sluggish healing wounds.

WELTMANN'S COAGULATION BAND IN PELVIC INFECTION.

The author first of all describes the test which consists of coagulating the proteins in diluted serum at different temperatures. This was found to be peculiar to groups of diseases. He himself carried out experiments on 53 patients and found that with marked inflammation of the uterine appendages the coagulation band was lowest. This was not so low in milder inflammation. With a change in the degree of inflammation there was an immediate alteration in the coagulation.

He concludes that this test is useful to confirm a diagnosis of pelvic infection.

THE ACTION OF ANTERIOR PITUITARY HORMONE ON NON-FUNCTIONING OVARIES.

The authors carried out a series of experiments on women after the menopause. They injected a dose of pregnancy 'urine intramuscularly before laparotomy. The urine contained about 5,000 mouse-units per litre. The ovaries were inspected at operation and investigated microscopically. The uterine mucosa was also histologically investigated. All gave nearly similar results, viz., that the injection of prolan did not stimulate a lost follicular function.

The uterine mucosa was characteristic for the age of the patient so that folliculin could not have been produced in the ovaries. There were neither ripe follicles nor corpora lutea in the ovaries.

A series of experiments carried out with women who had temporary cessation of ovarian function was attended with more encouraging results. These experiments were performed with cases of lactational and post-lactational amenorrhoea. The work is not yet complete and the author promises to publish his results later.

M. Datnow.

Munchener Medizinische Wochenschrift

September 18th.

*A new simple method of treating severe uterine haemorrhage. F. H. Bardenheuer.

October 17th.

*The importance of vitamins in the development and function of the female genitalia. Von. E. Gierhake.

October 30th.

*The ozone treatment of cystitis. Willy Bircher.

A NEW SIMPLE METHOD OF TREATING SEVERE UTERINE HAEMORRHAGE.

The author has recently treated some 230 cases of severe uterine haemorrhage by means of electro-coagulation applied in the uterine cavity. He refers to the history of the subject from the time when Pincus used steam. The method consists in the use of a special electrode for the uterus which has a coagulating ball electrode at its end and is insulated as far as this.

An indifferent electrode is applied to the leg. Prior to coagulating the mucosa, the uterus is curetted to exclude serious disease; this is best done some time before so that bleeding does not interfere with the coagulation. The indications are haemorrhage due to certain uterine myomata, pre-climacteric and climacteric bleeding, menorrhagia in young girls, metropathia haemorrhagica, and bleeding due to hypertension. The method is contra-indicated when there is any evidence of pelvic or adnexal inflammation, in the puerperium, and, of course, in cases of malignant disease. The complications are said to be few; there is usually a reactionary temperature and some pain; abscess in the pouch of Douglas, parametritis, and even uterine fistulae have occurred; the author himself has had one fatality.

THE IMPORTANCE OF VITAMINS IN THE DEVELOPMENT AND FUNCTION OF THE FEMALE GENITAL ORGANS.

The recent impetus of research on hormones and their chemistry is now leading on to the relation to vitamins. Some interesting statistics are quoted which were first published by Birnbacher in Vienna. He found that in conditions, e.g. xerophthalmia due to vitamin deficiency, apart from cases occurring during the first year of life, the percentage of occurrence was much higher in the male. In adults there were 101 cases in men compared with two in women. From this is deduced the observation that probably there is a higher immunity rate or storage in the female. Similarly, it is found that in vitamin E deficiency, whereas spermatogenesis is quickly affected in the male, in the female the sex cycle proceeds unimpaired but that a relative sterility owing to abortion or foetal death results. The author cites cases treated by vitamin E preparations with subsequent birth of a live child following previous stillbirths.

Deficiency of vitamin C is connected with hypoplasia of the uterus.

THE OZONE TREATMENT OF CYSTITIS.

The author has been impressed with the results of this treatment in a few cases in which he has tried it. All the patients had previously failed to respond to ordinary methods of treatment. The infecting organism was the bacillus coli: the urine rapidly became clear and was sterile in about three weeks.

R. K. Bowes.

Acta Obstetricia et Gynecologica Scandinavica.

Volume 16, Fsc. 3.

Becher's xanthoprotein reaction in pregnant and puerperal women. Finn Boe.

*A new method of diagnosis of rupture of the membranes. Claes von Numers.

Obstretrical anaesthesia with evipan. Ekkert Petersen.

*Pregnancy and labour in kyphoscoliosis. Björn Holmgren.

Fixation of the foetal head during pregnancy. Herbert Marcus.

A New Method of Diagnosis of Rupture of the Membranes.

Claës von Numers describes a simple method of diagnosis of rupture of the membranes depending upon the demonstration of fat globules in the vaginal discharge. A glass speculum is inserted a short distance into the vagina, a drop of secretion is then taken with a platinum loop and spread out on a slide previously rendered fat free. The slide is dried in the air and is stained without fixation at room temperature with a mixture of 0.2 to 0.3 gram of Sudan III in 100 cubic centimetres of 70 per cent alcohol. The slide is washed in water and dried with blotting paper before examination under a low power of the microscope. Fat is by this means stained a distinct orange red being much darker than mucus which is sometimes stained a weak yellowish red.

The writer examined 280 cases by this method, 141 before rupture of the membranes and 139 after rupture of the membranes. In the cases with unruptured membranes only four gave a very weakly positive reaction and the rest were negative, while in those with ruptured membranes only one case gave a negative result.

The writer considers this an easy method of determining whether the membranes have ruptured in a given case or not.

Pregnancy and Labour in Kyphoscoliosis.

Holmgren gives a comprehensive account of the 259 cases, previously published, of kyphoscoliosis complicating pregnancy and labour. Thirty-three of the patients died during pregnancy and 119 delivered themselves spontaneously with the subsequent deaths of 11. In this connexion he gives a complete list of references of all publications referred to in his text.

The writer himself has had the opportunity of observing 22 cases of high grade kyphosis or kyphoscoliosis with 29 pregnancies. Each case is described fully with X-ray photographs of its spinal deformity and photographs of some of the more pronounced cases are also added.

One patient in his series died during pregnancy from cardiac failure, four viable foetûs died and 13 patients delivered themselves spontaneously of living children.

Failure of cardiac compensation occured in four cases in which there was thoracic kyphoscoliosis. There was a contracted pelvic outlet in 11 cases of lumbar or sacral kyphosis. Abortion was therapeutically induced in two cases for active pulmonary tuberculosis and osseous tuberculosis respectively; spontaneous premature labour occurred in four instances; forceps delivery was called for on five occasions; the child was delivered by Caesarean section three times and the head of a dead foetus was perforated in one case.

The writer points out the special disability of the heart which is produced by spinal deformity in the thoracic region and the need for careful watch of the cardiac response to the strain of pregnancy.

The presence of contraction of the pelvic outlet did not, in his cases, lead to any difficulty in delivery. The cases reported by the writer were all kept under observation for a considerable time before delivery which in each instance was carried out in the Stockholm Maternity Hospital.

R. H. B. Adamson.

The Japanese Journal of Obstetrics and Gynaecology.

Vol. xix, No. 4, July 1936.

*A study of the gases in the umbilical blood. N. Noguchi.

On the maximal number of uterine contractions. H. Hori.

The effect of the functional abnormality of the maternal thyroid to the genital gland of the female foetus. T. Tanioka.

A Study of the Blood Gases in the Umbilical Blood.

Blood was aspirated from the umbilical vessels before and after respiration and a sample taken from the mother's blood at the same time. The oxygen and carbon dioxide were estimated by van Slyke's method. It was found that the onset of respiration markedly increased the oxygen content of the umbilical artery but the carbon dioxide content remained stationary. The blood from the umbilical vein showed no change after the onset of respiration. Thus it appeared that there was no disturbance of placental gaseous metabolsm after respiration commenced and therefore no evidence that a rise in the carbon dioxide content of the foetal blood is the stimulus to the respiratory centre for initiating the first respiration. The examination of the maternal blood showed evidence of the acidosis which is present at the end of labour.

An attempt to correlate the gaseous content of the umbilical vessels with the degree of asphyxia was made. In asphyxia livida it was found that there was either no alteration in the gas volumes or at the most a slight reduction in the oxygen content. In asphyxia pallida, on the other hand, there was a considerable reduction in the oxygen content and also a fall in the carbon dioxide content. Ante-partum passage of meconium was found in many cases in which there was no change in the gas valume but was present in all cases in which severe asphyxia existed. The author found no evidence than an accumulation of carbon dioxide in the blood acts acts as a stimulant to the sympathetic nervous system in promoting the passage of meconium.

R. J. Kellar.

REPORTS OF SOCIETIES

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY.

OCTOBER, 1936.

An Ordinary Meeting of the Society was held in the University, Manchester, on Friday, October 30th, 1936, with the PRESIDENT, DR. RUTH NICHOLSON in the Chair.

MR. PERCY MALPAS (Liverpool) read a paper on

ABNORMAL INCLINATION OF THE PELVIC BRIM AS A FACTOR IN DYSTOCIA.

The paper was based on a series of pregnancies in which apparent disproportion between the foetal head and the maternal pelvis at term was found to be due to an unduly high inclination of the pelvic inlet.

He considered that recognition of the obstetrical significance of the angle of inclination of the brim had been tardy, as, apart from a paper by Caldwell and Jacobs and a reference to the subject by Theobald in a recent discussion at the Royal Society of Medicine, little had been published on the subject. Hitherto interest in the pelvic inclination had centred either upon its anthropological significance or upon the bearing it had on the methods of determining the true conjugate diameter from the size of the diagonal conjugate. It was the two relatively new procedures of lateral X-ray pelvimetry and the lower segment Caesarean operation which had afforded opportunities for assessing the effect which an abnormal inclination may have on the mechanism of labour. The angle of inclination of the brim may be measured in two ways. The usual way is to measure the angle between the brim and the horizontal plane. There are two objections to this method. In the first place this angle is very much modified by posture and, therefore, does not readily lend itself to comparative purposes. The second objection is that it takes no account of the line of the lumbar spine, upon which much of the obstetrical importance of the inclination of the brim depends.

The other method of determining the inclination of the brim is to measure the angle between the plane of the brim and the front of the body of the fifth lumbar vertebra. This method is the one adopted on Dr R. E. Roberts's recommendation. The main advantage of using this angle as an index of the pelvic inclination is that it takes cognisance of the line of the lumbar spine. This point is rendered more clear if consideration is given to the conditions which obtain in the pelvis of the anthropoid apes. In the gorilla, for instance, the pelvic brim forms nearly a right angle with the horizontal, so that the pelvic inlet is directed almost directly backwards. This high

inclination, however, is offset by a forward crouch of the lumbar spine, so that the angle between the brim and the body of the fifth lumbar vertebra is reduced to about 100°, an angle which readily permits correspondence to be established between the uterine axis and the axis of the plane of the brim. It may be termed the angle of *obstetric inclination* of the pelvis, as opposed to that between the brim and the horizontal, which may be termed the angle of *postural inclination*.

The obstetric inclination varies with posture, but to a lesser extent than the postural angle. The average angle would appear to be about 130°, with a range of 10° to 20° with posture, full flexion of the legs and spine reducing it to 120°.

Accurate measurements are only possible by the use of X-rays, but a guide to the inclination is furnished by the inclination of the external conjugate diameter to the horizontal plane and the line of the lumbar spine. A high inclination of the external conjugate combined with a flattening of the normal lumbar curve would suggest a high obstetric inclination. The increased lordosis noted in many pregnant women is an indication of a postural compensation for the pelvic inclination.

Seven cases of apparent disproportion at term were then described, each of which presented two significant features. The first of these was that although the head was freely movable above the brim at the onset of labour, measurement of the biparietal diameter of the foetal head immediately after delivery showed it to be smaller in each case than the true conjugate of the brim. The second feature of the cases was an unduly high inclination of the brim. In five of these cases the head did not engage after some hours of labour and lower segment Caesarean section was performed. In a sixth case the first stage of labour was prolonged to forty hours, the second stage on the other hand lasted only an hour and a half. The child was stillborn. In the seventh case the most characteristic feature of the X-ray film was a marked lateral flexion of the foetal head on the spine. A living child was born by the natural forces after a prolonged first stage. Three cases were then described in which small pelvic measurements were found in association with a relatively horizontal pelvic brim. In each case, despite anticipation of dystocia, labour proceeded normally.

The general effect of high inclination of the pelvis is to disturb the normal correspondence which should exist between the axis of the inlet and the axis of the uterus. This reduces the effective size of the true conjugate diameter and also modifies the mechanism of labour so as to produce posterior asynclitism or Litzmann's obliquity, a noticeable feature in those cases which came to Caesarean section. This suggests that posterior asynclitism indicates failure to compensate the abnormal inclination. Lateral flexion of the foetal head upon the spine is one of the ways by which compensation is established. Its effect is to restore the normal synclitic relation between the head and the plane of the brim. The main problem in cases in which high inclination is present is how to restore correspondence between the axes of the uterus and that of brim. Theobald recommends pulling the uterus forwards during the pains. Caldwell and Jacobs recommend full flexion of the thighs, a posture

which has been shown to diminish the obstetric inclination. A somewhat similar position was indeed described by Smellie as long ago as 1766. Seeing that the effect of a high inclination is manifested in the first stage of labour uncomfortable postures are undesirable as leading to fatigue. A favourable posture in these cases would appear to be that which is spontaneously adopted by many women in the first stage of labour, the woman standing with the trunk leaning forward over a chair or the end of a bed, the arms or shoulders supporting the upper half of the body, the abdomen free so as to allow gravity to act on the uterus.

In general the main object of the paper was to demonstrate that every pelvic brim has a characteristic inclination as well as a characteristic size and shape, and the angle of inclination should be considered along with the other and better recognized factors when the management of a case of apparent disproportion is being planned.

Mr. MALPAS considered that the use of the procedure which we denote as trial labour was invaluable but in so far as the use of the term " trial labour " introduced the concept of unpredicted factors into obstetrics it was to be deprecated. It was the responsibility of obstetricians to eliminate as many unknown factors as possible. Some of the discredit into which pelvimetry had fallen, a discredit out of which the procedure of trial labour had developed, may have been due to concentration on only one of the characteristics of the inlet, namely its size, overlooking variations in inclination and shape.

The investigation depended largely on the radiological work of Dr. R. E. Roberts and Dr. P. H. Whitaker, to whom acknowledgments were made.

In the discussion which followed, Mr. Malpas was warmly congratulated on a most valuable paper.

PROFESSOR DOUGAL (Manchester) thought that an explanation was undoubtedly now afforded for certain cases in which the head overlapped though the pelvic measurements were normal.

PROFESSOR LEYLAND ROBINSON (Liverpool) drew attention to the fact that the pelvic inclination was greater than normal in the small round pelvis and less than normal in the flat pelvis, an additional reason why the former type of pelvis gave more trouble than the latter.

PROFESSOR MILES PHILLIPS (Sheffield) inquired as to the possibility of clinically detecting alterations in the pelvic inclination.

DR. GERRARD (Manchester) mentioned Jona's method in the estimation of the relative sizes of the head and pelvis, i.e. when the patient was made to sit up. It was noticeable that in quite a number of cases an apparent overlap was found to disappear, presumably owing to a lessening of the pelvic inclination.

MR. MALPAS in reply stated that the actual angle of inclination could only be determined by radiograms, but that an indication might be obtained when measuring the external conjugate diameter particularly when the patient had a straight back.

MR. T. N. A. JEFFCOATE (Liverpool) reported

A CASE OF ENDOMETRIOMA OF THE VULVA.

He considered the condition to be rare, in fact he had only been able to find reference to six other cases in the literature.

The patient, a nulliparous nurse, 45 years of age, complained of a small tender swelling at the posterior aspect of the right labium majus. This became so painful immediately prior to menstruation that it necessitated her leaving duty; she had also noticed a blood-stained discharge from the tumour during her menstrual periods. Her previous history was as follows. Menstruation began at the age of 19; it had always been regular, the loss lasting for five days and recurring every 30 days. In 1931 a cyst of the right Bartholin's gland was excised in Athens. Slight pyrexia followed this operation, but healing was not delayed. The operation was performed 12 days before menstruation, and local anaesthesia was employed. It was almost certain that curettage was not performed. A month later an abscess appeared under the scar and was incised. Seven further abscesses developed in the ensuing six months; they were treated by fomentations. In May 1932, a further operation was performed at Athens for an inflammatory swelling; the contents of the swelling were aspirated and tincture of iodine was injected at the same time. In June 1932, a gland and abscess were excised at Marseilles. The incision was closed but suppurated, and an open wound resulted. The patient began to menstruate two days after the operation. This wound never completely healed and always bled a little prior to menstruation. The small lump appeared four months after operation: it was obvious only after menstruation, and gradually disappeared in four or five days. The patient first consulted Mr. Jeffcoate in June 1936, i.e., four and a half years later, her symptoms having been present during the whole of the intervening period.

On examination there was considerable scarring at the posterior aspect of the right labium majus, and beneath this was a small hard tumour with a depression and reddening over it. The uterus was retroverted but there was no other pelvic abnormality. The tumour was excised; it contained small blue cysts, one of which burst during the operation and discharged a small quantity of old blood. The incision was completely healed 15 days after the operation; the symptoms had not returned. The specimen removed on the seventeenth day of the menstrual cycle was a roughly spherical tumour of three-quarters of an inch in diameter, with two or three small cavities containing blood.

Microscopic examination revealed typical endometrium in the interval phase presenting the appearances of hyperplasia.

Mr. Jeffcoate thought that the tumour had undoubtedly arisen as the result of implanation of endometrium. It would appear that curettage had never been performed, and he believed that the endometrioma had developed from endometrial cells present in the menstrual blood. From the history it seemed most likely that implantation had occurred immediately after the third operation, as on that occasion the incision had completely broken down,

exposing a large cavity, and menstruation had occurred within a few days of the operation. The case was deemed to be similar to those previously recorded in that implantation of endometrium from the menstrual or lochial discharge had been the mechanism of origin.

PROFESSOR D. DOUGAL (Manchester) reported

A CASE OF ARRHENOBLASTOMA OF THE OVARY.

In June of this year he had been asked by one of his colleagues on the medical side of the Manchester Royal Infirmary to see a girl, aged 18 years, with the following history:

Menstruation commenced at the age of 13 and continued every 28 days with a normal loss lasting four days, until she was aged 16½ when the periods ceased. The patient then noticed that her voice was becoming deeper in tone and that hair was appearing on the face and other parts of the body where it had not hitherto been present. She also developed acne and was treated with X-rays, without deriving any benefit.

About the same time her sella turcica was radiographed with a negative result.

On examination he found her to be a young woman of average stature but presenting well marked male secondary sexual characteristics. Her face had an unhealthy appearance due to acne, and hair was present on the cheeks, upper lip and chin. The breasts were flattened and atrophic, the nipples shrunken and several hairs were growing on the areolae. Hair was also present on the front of the chest, the anterior abdominal wall, and the anterior surfaces of the thighs and legs.

The pubic hair was very abundant and of male distribution, extending upwards in the mid-line above the umbilicus and backwards over the perineal and anal regions.

The general appearance of the body was masculine, there being little subcutaneous fat and no rounded contours.

The external genitals were small, with the exception of the clitoris and prepuce which were much hypertrophied and measured over an inch in length. The orifice of the vagina was extremely small, the vaginal canal narrow, and the body of the uterus definitely atrophic.

No definite tumour could be made out in the renal or hypogastric regions, but it was noted on bimanual examination that the right ovary was somewhat enlarged. As it appeared possible that this enlargement might be caused by a new growth, it was decided to examine the patient under an anaesthetic. This was done but little more information was forthcoming.

The girl's parents were interviewed and the position explained to them. It was pointed out that as a very small tumour might be present in the ovary it was well worth while exploring the abdomen as the removal would probably result in a complete cure. Consent was immediately given, and on June 12th the abdomen was opened. The right ovary was found to be about the size of a walnut and fairly firm in consistence. The body of the uterus was definitely atrophic but the other ovary appeared to be normal in size. The right ovary was removed.

The patient made an uninterrupted recovery. During her three weeks in hospital there was a definite though not dramatic change in her appearance.

She was seen again on August 11th, two months after the operation. She said that she had had a normal menstrual period on July 19th.

Her complexion was much clearer and there was less hair on the face, chest and abdomen. The breasts were larger and the clitoris definitely smaller.

By October 28th there was still further improvement. Menstruation was now regular every 28 days, the duration being six days. There was a definite increase in weight and the contours of her body were becoming more rounded.

The hair on the face had largely disappeared, and although still present on the abdomen and thighs was scantier and of finer texture.

The breasts were now well developed and firm.

The clitoris was very little larger than normal and the uterus appeared to have regained its proper size. The voice was still deep but its tone was definitely higher than before the operation; this point was demonstrated by gramophone records.

The patient was well satisfied with her progress and asked if she might marry. She said that she had been engaged to be marreid for about three years, and on further questioning stated that she had noticed no change in her feelings towards the opposite sex since the cessation of her menstrual periods.

The specimen removed consisted of the right ovary which was about the size of a walnut. On bisecting the organ the enlargement was seen to be due to a solid tumour of softish consistence and olive green in colour. The tumour was quite distinct from the ovarian tissue proper which surrounded it in the form of a thin shell.

Microscopic sections showed a richly cellular growth with varied appearances in different parts of the tumour. In some places the cells were arranged in cords, in others the arrangement was trabecular, in others again it was diffuse resembling sarcoma.

Although the macroscopic appearance suggested the presence of fat, sections stained with Sudan III showed no evidence of this.

The arrhenoblastoma is the musculinizing tumour, like the granulosa-cell tumour and disgerminoma it is believed to arise from rests of the primitive mesenchymal cells of the gonad. It is usually unilateral and its malignancy, if it possesses any, is of a very low degree so that in young women at any rate it is not necessary to remove the uterus and both ovaries.

It is also extremely rare, only 26 cases having been published up to 1933.

With the increasing interest in these special ovarian tumours, however, it seemed likely that a great many more would appear in the literature before long.

The case was discussed by several members of the Society, and there was some difference of opinion as to whether or not the patient's voice had changed as a result of the removal of the tumour. The opinion was expressed by a number of speakers that a change in the voice was hardly to be expected in view of the largely cartilaginous structure of the larynx. Cases had

been reported, however, in which it had definitely been stated that the voice had altered its character.

MR. T. F. TODD (Manchester) showed a specimen of

AN EARLY CHORION-EPITHELIOMA.

The patient, who had had two children, was aged 31; she was first seen two months ago on account of a severe vaginal haemorrhage. The history was that she had spontaneously expelled a hydatidiform mole, after threatening to abort for a week previously, three weeks before Mr. Todd saw her. Following this she had been pyrexial for several days, but otherwise had no particular symptoms. Exactly three weeks after the mole was expelled she had a severe flooding, losing two or three pints of blood.

On examination she was found to be considerably anaemic, with a pulse-rate about 110. The uterus was slightly enlarged, and there was quite brisk haemorrhage from the external os. Curettage was obviously called for, and she was immediately anaesthetized. The cervix was dilated; on digital exploration of the uterus a mass of tissue was found projecting into the cavity on the left side. This mass was firmly attached to the uterine wall; a plane of cleavage was not found, as it usually is with retained products of conception. The presence of this phenomenon coupled with the history of a hydatidiform mole three weeks previously, led to the diagnosis of chorion-epithelioma. Curettage was out of the question, and in view of the free haemorrhage and the patient's poor condition, it was decided to remove the uterus forthwith, without waiting for the pathologist's confirmation of the diagnosis. Vaginal hysterectomy was speedily effected and the patient returned to bed in a condition not much worse than that in which she left it. The ovaries and Fallopian tubes were not removed. Mr. Todd was not at all convinced that this was really necessary; if not, then it was much better to leave the ovaries at her age. On examination of the specimen it was interesting to note that there was no suggestion of a follicular cyst in either ovary. The growth could be seen on the left side of the uterine body approximately in the middle of the specimen. Its macroscopic appearances were those of a typical chorionic growth, and the reason the specimen was shown was because the pathologist's report stated that it was the earliest specimen he had yet seen microscopically. The histology confirmed the clinical diagnosis, and nowhere could any suggestion of invasion of any vessels be determined.

It was presumed that the prognosis in such a case was excellent. Both macroscopically and microscopically the growth was an early one, and it had been removed *in toto*. The patient made an uninterrupted recovery; when examined recently there was no abnormality to be seen, nor had she developed any cough. It was proposed to examine her regularly for at least a year to be sure that no metastases developed and to be able to treat them should any appear.

Discussion. MR. DATNOW (Liverpool) said that Mr. Todd's case of chorion-epithelioma interested him from three points of view.

(1) *Diagnosis.* Here great assistance was given by the Zondek–Aschheim test. In doubtful cases it was of value to dilate the cervix sufficiently to introduce the finger into the uterus; in this way, it was often possible to feel an early growth which is missed by the curette. The histological picture of curettings is sometimes difficult to interpret, and he had frequently seen equivocal reports as the results of simple curettage.

(2) *Treatment.* It was not wise to remove the uterus by the vaginal route for any form of malignant disease of the uterine body, because there was too much handling of the organ with possible dissemination of the growth through the Fallopian tubes and the blood-stream. It was not so easy to remove the appendages which should not be left because their lymphatics were so intimately related to those of the uterus.

(3) *Prognosis.* Here Mr. Datnow thought the Zondek–Aschheim test was invaluable as it invariably became negative if the growth was removed from the patient's body, whereas a positive result invariably meant that there were metastases. He had followed a case after operation with the Zondek-Aschheim test and found that positive results were obtained with increasingly greater dilutions of urine as the metastases progressed and extended.

Dr. I. A. B. Cathie (Manchester) who had made the pathological report on the case, stated that he was inclined to consider the specimen as being really in the nature of a syncytioma.

Mr. Todd in reply agreed that chorion-epithelioma was preferably treated by abdominal hysterectomy. The vaginal operation had been carried out in this particular case owing to the extremely poor condition of the patient.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY.

NOVEMBER, 1936

A meeting of the Society was held in the University, Sheffield, on Friday, November 27th, with the President, DR. RUTH NICHOLSON, in the chair.

A discussion was held on PROFESSOR A. M. CLAYE'S paper on

CAESAREAN SECTION. WHAT ARE THE INDICATIONS?

presented at a previous meeting of the Society.

Professor Claye had stated that the indications for Caesarean Section had been until fairly recently:

(1) Contracted pelvis
(2) Tumours obstructing labour.

There were certain considerations with regard to the classical operation.

(*a*) High mortality. At the optimal time the mortality was 1.5 per cent; late in labour it was 9.4 per cent; after attempts at vaginal delivery 26.5 per cent.

(*b*) The uterine scar was potentially weak with a tendency to rupture should subsequent delivery by the vaginal route be attempted.

(*c*) Should uterine infection occur, general peritonitis might result with a consequently high mortality. For this reason craniotomy was reputed to be safer than late classical Caesarean section.

With the lower segment operation the situation was different.

(*a*) A comparatively low mortality. Professor Claye quoted the figures of Bailey, Evers, Marshall, Walsh and the Leeds Maternity Hospital, giving a mortality of 1.6 per cent in 559 cases; many of the Caesarean sections were performed late in labour or after interference. The operation was undoubtedly much safer than craniotomy; the mortality of the latter operation, from representative hospitals, was 9 per cent.

(*b*) The scar in the lower uterine segment was much less dangerous than that in the classical operation.

Professor Claye wondered in view of the good results obtained by lower segment Caesarean section whether the indications should be widened. There seemed to be no reason for confining Caesarean section to one dangerous cause of delay, i.e. contracted pelvis.

He thought it might be used occasionally in cases of primary uterine inertia, including colicky uterus or in poorly flexed occipito-posterior cases in which mother and child might be in danger long before full dilatation of the cervix. Caesarean section in such cases carried less risk than trachelotomy or manual dilatation of the cervix.

Other indications in a series of lower segment operations he had performed,

were cardiac disease, brow presentation, fibroid, scarred cervix and carcinoma of the cervix. Caesarean section and sterilization were performed in cases of cardiac disease if the patient was considered fit to stand the operation, but not fit to endure another pregnancy.

In a series of cases of classical Caesarean section, the indications, other than contracted pelvis, were placenta praevia, fibroids, toxaemia, accidental haemorrhage, repeated transverse lie of the child, previous complete perineal tear, previous puerperal insanity, breech in an elderly primigravida, and repeated prolapse of the umbilical cord. Professor Claye felt that Caesarean section on certain of these indications was justified only on rare occasions. In placenta praevia, for example, Caesarean section is considered if the patient is a primipara in good condition, the child alive and well developed and the placenta central.

Professor Claye stated that it was often said that it was important to preserve the obstetric art, and that if all difficulties were treated by Caesarean section, the art would disappear. He did not suggest that all difficulties should be dealt with by Caesarean section, but only a few carefully selected cases. He thought that our primary object in obstetrics should not be the preservation of the obstetric art, but to obtain the best possible results for mother and child irrespective of method.

The discussion was opened by MR. W. GOUGH (Leeds) who stressed the dangers of the unnecessary performance of the operation. He deplored the growing tendency to treat any obstetric difficulty by Casarean section as the first line of treatment when it when it should really be the last line. The operation, though easy, was by no means trivial, and a low maternal mortality was not the sole criterion of success. There was always the possibility of subsequent disability from, for example, adhesions, hernia or fistulae. He felt that Caesarean section could rarely be justified as a method of treatment of primary uterine inertia though no doubt every obstetrician could look back on cases in which he had eventually wished that he had performed Caesarean section.

The trouble was that he could never foresee how any given case would finally turn out. As a rule, however, they did well without interference. When fibroids were present, it was advisable to wait until the patient was advanced in labour, because fibroids often went up out of the way as the lower segment was taken up. Mr. Gough did not himself perform Caesarean section in frank breech cases unless the pelvis was contracted. He made use of the operation in picked cases of placenta praevia but did not agree to it as a routine. He rarely adopted it as a method of delivery in cardiac disease.

The PRESIDENT drew attention to the fact that the number of Caesarean sections for contracted pelvis was being reduced by making use of trial labour followed by the comparatively safe lower segment operation in cases of failure. She thought that there was a place for Caesarean section in the case of an elderly primigravida with a large child.

MR. A. GOUGH (Leeds) made the point that in a given case the indications for Caesarean section were often multiple.

He quoted the case of a primigravida of 44 years of age, a fortnight past her calculated date, with a large child, a slightly diminished conjugate diameter and rigidity of the soft parts. None of these factors by itself would be sufficient to justify Caesarean section, but taking them all into consideration one would not hestitate to operate. With regard to uterine inertia he could not accept that alone as a sufficient indication. Occasionally, however, the presence of other abnormalities such as disproportion, toxaemia or placenta praevia might serve to turn the scale in favour of operative delivery.

Dr. C. H. Walsh (Liverpool) reviewed a long series of cases of Caesarean section performed at the Mill Road Infirmary and Smithdown Road Hospital, Liverpool. He preferred the lower segment operation except in cases in which large veins were present. He considered that Caesarean section was rarely indicated in cardiac disease.

Mr. St. George Wilson in reference to trial labour thought that the usual approach to the question as an anatomical consideration of the presenting part and the pelvis was quite wrong. The test was really a physiological one. He also thought that the term "uterine inertia" could with advantage be replaced by the more expressive term "disordered uterine action".

Mr. P. Malpas (Liverpool) considered that a discussion of massed results of Caesarean section possessed little advantage. Every obstetric case presented individual risks and problems, and the selection of Caesarean section as the method of delivery must be based on a consideration of the dangers and results of all the other methods available in the particular case—natural forces, forceps, version, embryotomy.

The lower segment operation, while minimizing the incidence of puerperal infection, did not confer absolute immunity against peritonitis. There were some cases in which the protection afforded by the lower segment operation should be supplemented by drainage.

Mr. C. M. Marshall said that it was now about one hundred years since Baudelocque had expressed the opinion that Ceasarean section was being performed much too frequently. Almost every authoritative statement since that time had been prefaced by remarks of a similar kind. Mr. C. G. Walsh's excellent figures were only some of many that showed conclusively that the modern improvements in the operation were greatly increasing its safety. It was only natural that a somewhat wider scope for its application should develop. He thought it would be safer to explore all the possible ways in which the technique of the operation could be improved. He had now carried out the lower segment operation in 170 instances without maternal mortality. Spinal anaesthesia, though its risks were higher in this than in other pelvic operations, endangered the life of the mother much less than general anaesthesia. In all severely ill women, whose reactions to lumbar anaesthesia were uncertain, he now employed local anaesthesia. The outstanding results recently published by Daily from the Chicago Lying-in Hospital clearly showed the decided advantage which would follow a wider adoption of this latter method. The speaker then referred to some special points in the technique when using the lower segment operation in placenta praevia. After the

abdomen had been opened, the presentation was converted to a breech and then making a small transverse incision in the lower segment, a leg was pulled through. Traction on the leg was kept up while the uterine incision was being extended, and in this way complete control of the haemorrhage could be obtained. If the breech could not be made to present and the initial small incision involved the placental site, the wound should be quickly extended with the index fingers, the hand inserted, and a leg secured.

Dr. E. A. GERRARD (Manchester) made reference to Banister's contention that only in 50 per cent of cases do women who have had a Ceasarean section performed subsequently become pregnant. He thought that this point was all too frequently overlooked.

Professor CLAYE, in reply, emphasized that he considered Caesarean section the right treatment for primary uterine inertia and for occipito-posterior position only in the rare cases in which maternal or foetal distress was present with a partially dilated cervix. He used the term *inertia* to include any cases with inadequate pains in which there was no other evident cause of delay. He congratulated Mr. St. George Wilson on his definition of trial labour.

ROYAL SOCIETY OF MEDICINE

Section of Obstetrics and Gynaecology

A meeting of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine was held on Friday, November 20th, 1936, when a discussion was held upon

The Present Position of the Hormones in Gynaecology and Obstetrics.

Professor E. C. Dodds first showed a diagram demonstrating the relation between the hypophysis, the ovary, the testis and the other glands of internal secretion. He emphasized the fact that myxoedema might occur in association with gynaecological conditions, and that some of the failures which were seen with oestradiol and progestin could be overcome by the combined use of thyroid, which increased the sensitivity of the patient to these hormonal derivatives. He hoped a time would shortly arrive when the hormones on the market would be standardized and measured in weights, e.g. milligrams rather than units, now the constitution of these crystalline substances was known. He laid stress upon the fact that oestrone and its derivatives have no carcinogenetic activity whatever when tested in the same way as carcinogenetic hydrocarbons, a fact of some import, which was corroborated by the excellent results obtained in the treatment of kraurosis vulvae, a condition which pathologists regard as precancerous. Finally, he paid tribute to the labours of chemists and biologists who have produced the sex hormones.

Dr. H. Gardiner-Hill said it was important to remember that endocrine therapy is essentially substitution therapy, and that endocrine extracts do not stimulate the specific glands which secrete them. We must not, therefore, expect too much from anterior pituitary therapy. Moreover, the gonadotropic substances so far available are only anterior pituitary-like substances which have been extracted from pregnancy urine, and only stimulate the interstitial cells of the ovary. Dr. Gardiner-Hill then reviewed the functions of the sex hormones, and stated that he thought that ovulation was under the control of the anterior pituitary. He next dealt with the sexual development of cases of delayed puberty and infantilism. They can be divided into three types: (1) hereditary; (2) cachectic; (3) endocrine. He stressed the point that treatment for such conditions was essentially a substitution therapy, and produced no permanent results. He thought that sterility of endocrinal origin was not uncommon, indicating that treatment with thyroid extract was often useful, but, of course, the majority of cases were probably due to anterior pituitary deficiency and failure of ovulation. Such cases were difficult to treat because anterior pituitary hormones are not yet available.

As regards pregnancy, he considered that repeated miscarriages were frequently due to poor conditioning of the endometrium, the result of athyroidism or deficiency of progestin. He was of the opinion that the menopause offered the most fruitful field for oestrogenic treatment.

Mr. JEFFCOATE stated that there was a tendency to paint the lily; this attitude might do harm and interfere with progress. He was of the opinion that the treatment of functional haemorrhages by organotherapy or progestin was almost useless, and he showed tables to prove this, though he admitted pre-pubescent cases did benefit. He showed that oestrin therapy was very valuable in those cases in which the foetus was dead and retained; spontaneous expulsion could be expected by increasing the uterine sensitivity to folliculin. The dosage was 40,000 units eight-hourly for five days if need be, and then labour pains are induced by the routine castor-oil-quinine technique. His personal success was 80 per cent. Speaking next of uterine inertia, he admitted that such cases were difficult to assess, yet his own impression from hospital and private work was that the injection of 20,000 units every hour for 10 hours was of great use in at least 50 per cent of cases. He commended oestrin therapy for trial in cases of amenorrhoea, sterility, vulvo-vaginitis and dysmenorrhoea.

Mr. T. N. MACGREGOR spoke of the pubescent and young adolescent haemorrhages, and stressed the importance of pathological report upon the endometrium in such. Some are due to a failure of follicular ripening subsequent to anterior pituitary underfunction; others to endometrial hyperplasia. He was optimistic of the future rôle which may be played by sex hormones in these states. He was a believer in the value of hormonal urinary and haematological analyses, though he admitted that the majority of cases of amenorrhoea were due to pituitary underfunction, and, therefore, can now be treated by pregnant mare's serum which is on the market. If, on the other hand, biological analysis showed that overfunction existed, then he advised oestrogenic treatment.

Dr. P. BISHOP stated that recently he had been using the vaginal smear method of Papanicolaou for assessing the oestrin index of patients, both before and after treatment. It is an easy way, and it had shown that quite small doses, such as 1,000 to 5,000 units, had a marked effect upon the vaginal mucous membrane. He spoke of the variability of response of the tissues in the female to circulating oestrin; this depends upon the capacity for utilization, which again probably depends upon the autonomic nervous system. He next spoke of the transitory effect of oestrin in cases of amenorrhoea and emphasized the importance of inhibitory stimuli from the hypothalamus in some cases. He mentioned metropathia haemorrhagica as an instance of the beneficial effect of progestin and its capacity of lowering the level of oestrin which can be utilized by the endometrium; but in how many was the case cured or the benefit lasting? He considered that quite small doses by mouth, such as 5,000 units of oestrin, were of great value for many of the troubles met with during the menopause. He deprecated excessive enthusiasm and excessive scepticism.

Mr. CHASSAR MOIR said that he wished to make a plea for a more critical attitude in interpreting the results of the treatment of gynaecological conditions by hormone therapy. Some figures had been mentioned in which success had been claimed in an exact percentage of cases without, it seemed, due consideration having been given to the likelihood of the disordered

function spontaneously reverting to the normal. The length of time for which the abnormality had been established, and the speed or otherwise of the alleged remedy in effecting a cure, were points which were also given insufficient attention. He hoped that when the papers appeared in print fuller details would be forthcoming regarding the standards by which success and failure were judged. Excessive menstrual bleeding at puberty offered an example of the particular type of difficulty inherent in this type of experimental treatment. With the lapse of time such cases, in the vast majority of instances, underwent a spontaneous cure; keeping this in mind, was it reasonable to claim success in a case in which progesterone or prolan had to be continued over a period of, say, six months before a diminution in the uterine haemorrhage occurred? While he fully realized the great difficulties in this type of work, he ventured to suggest that the claims for endocrine therapy in the treatment of menorrhagia would be much more convincing if the cases included in statistics were limited to those in which the patient had suffered from the abnormal condition for a period of at least six months, and success in this type of therapy claimed only when a definite improvement set in within six weeks of the institution of the treatment.

Mr. DONALDSON said that in his opinion the average gynaecologist had neither the time nor the facilities to do clinical research on hormones. He therefore advocated that a centre should be organized in London where there were sufficient beds ear-marked for the purpose and sufficient laboratory facilities really to carry out intensive research on the subject of hormones. The present haphazard way of doing this work could only lead to results which would prejudice organotherapy.

Professor JAMES YOUNG stated that this discussion had demonstrated very clearly that there were several ways in which hormones had established for themselves a position of value in obstetrics and gynaecology. He believed that it was important that this should be clearly realized by members of the profession because there were still those who, influenced by the somewhat unsavoury reputation which this subject had claimed in the past, were inclined to refrain from their employment altogether. He pointed to the evidence which had completely established their place in the treatment of the vasomotor symptoms of the menopause, the chronic irritative vulval lesions occurring after the menopause, and habitual abortion. His own experience with hormones in irregular and excessive uterine haemorrhage had not been satisfactory, but the records of Dr. Jeffcoate were so good that he felt encouraged to give this line of therapy a further trial. It was obvious that if we could obtain a 60 per cent clinical relief in these conditions, a figure which Dr. Jeffcoate had achieved, we had at our disposal a weapon of very great value. In connexion with the use of the hormones there were one or two notes of warning which might be worth uttering. For example, when he had employed massive doses of oestrin for cases of kraurosis and leukoplakia he had in two instances, in comparatively old women, found a very marked painful distension of the breasts induced; then, in the employment of the luteal hormone for cases of habitual abortion, he had in one instance seen a case in which the prolonged employment of

the drug had led to pregnancy continuing for several weeks beyond term. This resulted in the birth of a very large child which was born dead. On this occasion the patient had passed out of his observation during the latter months of pregnancy. The possible occurrence of such a disaster pointed to the importance of careful supervision, and to the cessation of the therapy before term.

The Edinburgh Obstetrical Society

At a meeting ol the Society held on 11th November, 1936, Dr. DOUGLAS MILLER delivered the Presidential Address on

THOUGHTS ON THE LIFE AND WORK OF SIR JAMES YOUNG SIMPSON.

After a brief description of Simpson's youth and undergraduate career, Dr. Miller referred to Simpson's early postgraduate training, and in particular to his work as assistant in the Department of Pathology under Professor Thomson, in whose association he found one of the great formative influences of his life. It was here that he formed the Hunterian "don't think but try" attitude of mind; it was here that he developed habits of accurate observation and lucid description; and it was Thomson who urged him to turn his attention to obstetrics.

At the age of 28 Simpson was appointed to the Chair of Midwifery, and proved to be one of the greatest teachers in the history of obstetrics. He possessed in full measure the qualifications which Osler said the good teacher must possess—the ability to bring an atmosphere of enthusiasm into the class-room, a full and personal knowledge of his subject, and a sense of obligation which compelled him also to be a contributor. Within a few years the class of midwifery became for the first time in its history the largest in the University, attended daily not only by students, but by graduates from all over the world.

The discovery of the anaesthetic property of chloroform was, of course, Simpson's chief claim to the grateful remembrance of posterity. As a student his sensitive nature had been so revolted by the barbarous cruelty of an operation, performed, of course, upon a fully conscious patient, that he had seriously contemplated giving up medicine in favour of law as a career. On that day he had formed the resolve to discover a means whereby the suffering which surgery then entailed could be avoided, and all his thought and energy were consecrated to this end. From the earliest dawnings of history painless surgery was an ideal which had occupied men's minds, and from time to time patients had been made insensible by drugs and vapours of various kinds. No anaesthetic agent of sufficient merit, however, had been found to compel general acceptance, until on October 16th, 1846, Morton, of Boston, demonstrated the anaesthetic properties of ether in such a way as to convince the medical world. Three months later the first maternity patient in whom a general anaesthetic had ever been employed was delivered in Edinburgh under Simpson's care. This

was an epoch-making advance, but Simpson was not satisfied that ether was the ideal anaesthetic for his purpose. He wanted, if possible, to find a substance more rapidly analgesic, more portable and less unpleasant to inhale; after further research, in which self-experimentation played an important part, chloroform was discovered on November 4th, 1847.

Dr. Miller then referred in some detail to the more important contributions which Simpson had made to the knowledge both of obstetrics and of general medicine, and in particular to his work on delayed labour, on puerperal sepsis, and on hospital construction. A comparative study of the practice of obstetrics in 1840, when he was appointed to the Chair, with that of 1870, the year of his death, left one with the conviction that with the notable exception of Listerism, the advances which were made during Simpson's professional lifetime were as great in extent and importance as those which had been made since his death, and further that much of this improvement in the standard of practice was due to his own observations and teaching.

If an attempt were made to analyse those factors, other than home influences, which specially contributed to his greatness, one found that there were three which might be briefly considered. First, an intellect of quite exceptional calibre. His studies on anaesthesia, on delayed labour, and on hospital construction all gave abundant evidence of originality and of profound thought directed along essentially practical lines. He was at once a master of obstetrical strategy and a brilliant exponent of tactics and technique. The second factor in Simpson's success was that complex quality, termed personality, of which in this case the chief components were an intense vitality and an ardent enthusiasm. The third factor, and perhaps the most important, was his capacity of intense concentration and unremitting hard work. His work had the dual qualities of thoroughness and zest, so that whatsoever his hand found to do he did it with all his might. His interest in his vocation amounted to an all-absorbing passion so that it seemed to come naturally to him to "scorn delights and live laborious days". No one did more than he to establish obstetrics as a science as well as an art, but the debt we owed him was to be measured not only by his contributions to our knowledge, but also, and even more, by the example he gave us of an enthusiasm that never languished, of an energy that never wearied, and of a life-long devotion to the highest ideals of our profession.

ROYAL ACADEMY OF MEDICINE (IRELAND)

A meeting of the Section of Obstetrics of the Royal Academy of Medicine in Ireland was held in the Royal College of Physicians on Friday, October 16th, 1936; the President, DR. J. F. CUNNINGHAM, was in the chair.

A discussion was held on

PUERPERAL SEPSIS.

DR. A. H. DAVIDSON gave an account of an outbreak of haemolytic streptococcal puerperal infection which occurred in the Rotunda Hospital in the spring of 1936; there were fourteen cases of sepsis, with four deaths. It was coincident with a severe epidemic of streptococcal pharyngitis in the hospital and in the city, and also with a number of structural changes taking place in the hospital buildings.

Swabs were positive for streptococcal infection in all cases, and blood-cultures were taken from eight patients; these were found to be positive in two; both patients died. Throat swabs were positive for haemolytic streptococcal infection in seven cases. Ten cases had spontaneous births, and in seven cases there was no vaginal interference of any kind. Eight of the patients were in direct contact with droplet infection from a doctor or nurse whose throat swabs were positive for haemolytic streptococci. Three patients developed peritonitis; two died and one recovered. The abdomen was opened and drainage tubes inserted in each of these three cases. None of them had a positive blood-culture. Three patients developed insanity.

The treatment consisted in the administration of polyvalent antistreptococcal serum, antiscarlatinal serum, and intra-uterine glycerine when the lochia were purulent or foetid, and routine nursing measures. Prontosil was used only in the last case with satisfactory results. It was not available in the earlier cases. The cases were isolated in a large ward with separate staff, crockery, dressings, etc. All the nurses, students and staff of the hospital had their throats swabbed and any persons with positive swabs were sent home or off duty. Vaginal examinations were completely stopped and all operative intervention reduced to a minimum. Masks were worn in the labour ward and lying-in wards.

The importance of spray and droplet infection was well borne out in this epidemic and shows the necessity of early recognition and segregation of those with infected air passages.

Dr. R. M. CORBETT reported

AN OUTBREAK OF SIX CASES OF PUERPERAL INFECTION OCCURRING IN THE COOMBE HOSPITAL

at the beginning of June, 1936.

In one of these cases, streptococci were grown from the blood and in two, from the uterine swabs. In the four others, although streptococci were

seen in the smears from the uterine cavity, no organisms could be grown aerobically. In these four cases large quantities of pus formed in the uterine cavity, yet no growth could be obtained.

The cases were treated with prontosil by intramuscular injection and by mouth; intra-uterine douches were given when any quantity of pus was found in the uterine cavity. All the patients survived.

No conclusion as to the origin of the outbreak was reached, but, at the same time, one patient in the hospital had an acute streptococcal infection of the throat, three nurses were off duty with sore throats, and one nurse with scarlet fever; swabs from the throat of the staff showed haemolytic streptococci in the throats of one assistant and 14 nurses. The patients, who were infected, had all been in contact with, at least, three nurses carrying haemolytic streptococci.

The usual precautions of isolation and the elimination of carriers of active streptococci were taken.

Dr. J. S. QUIN read a note on

AN UNUSUAL CASE OF PUERPERAL INFECTION.

Dr. F. W. DOYLE and Dr. R. V. MURPHY described

A CASE OF SUB-ACUTE ENDOCARDITIS

recently encountered by them.

The feature of the case was an old standing mitral stenosis, with pyrexia and tachycardia continuing for almost six weeks after delivery. The patient was a multipara, delivered by forceps, under gas-oxygen anaesthesia. The treatment included the exhibition of anti-streptococcal concentrated polyvalent serum, anti-anaemic therapy with salicylates, and, later, the administration of digitalis.

The patient's condition slowly improved from the sixth week, and, except for a rather persistent tachycardia and attacks of dyspnoea, she remains comparatively well.

The PRESIDENT said that it was unusual to get four communications on the same subject for discussion on the same evening, two of which came from the Masters of the Maternity Hospitals in Dublin. He congratulated the Masters on the steps they had taken to deal with the outbreaks, and the success which they had achieved.

Dr. G. C. DOCKERAY said that during the epidemic at the Rotunda Hospital the rule had been introduced of taking a swab from anyone in the hospital who had the least sign of a cold in the head or a sore throat, and this would be continued in the future. It was very important, however, to see that no nurse was allowed to return to duty in the hospital until a release swab had been taken. Dr. Colebrook had recently stated that in his experience about 50 per cent of cases died of streptococcal septicaemia, and many of them were contracted from sore throats. It should be remembered that haemolytic streptococci might be present in the air. At the Rotunda Hospital no anaerobic cultures had been grown, as it was

obvious that they were dealing with an outbreak of haemolytic streptococcal infection. There was more difficulty about taking blood-cultures than about taking throat swabs, as cultures had to be put into anaerobic media. He was of opinion that in the next copy of the rules of the Central Midwives Board sore throat should be specifically mentioned. Streptococci should be grown on broth and on the sugar trecolose; if it fermented trecolose it probably was not pathogenic. In some long-standing cases in which one was uncertin how to proceed he thought it a mistake to employ too few therapeutic measures.

Dr. C. J. McSweeney said he saw a good many cases of puerperal sepsis in Cork Street Fever Hospital. Since September, 1934, they had treated there 52 cases. Twenty were cases of pure septicaemia; eight of these died. In all the fatal cases a pure culture of haemolytic streptococcus was obtained from the blood. There were two cases of pyaemia, both of which recovered. Of the 30 remaining cases none died. These cases were of various types. Out of the 52 cases eight died. He was of opinion that the place of surgery in the treatment of puerperal sepsis was very limited. There was really no treatment of puerperal sepsis because it was not a clinical entity, and every case had to be treated on its own merits. Conservative treatment was undoubtedly the best. The only serum of value in treatment was scarlatinal anti-toxin, which must be given in big doses, and given repeatedly. In selected cases glycerine was very useful, especially in local pelvic conditions. Collosol iodine as an adjuvant to serum was useful. No other drug had been found to be consistently of service in the treatment of this condition. He thought that some cases were discharged too soon from the maternity hospitals, especially patients who had to return to the slums of Dublin where conditions were so unfavourable. Cases of puerperal septicaemia were much more the result of endogenous infection than exogenous. In this connexion he would utter a plea for small septic wards in hospitals. He hoped that hospital administrators would soon realize that the building of wards had a great deal to do with infection. He felt that the day of the large ward was gone. Small wards and aseptic nursing were absolutely necessary in every hospital. No mask was of any use at all except a cellophane one. Gauze masks quickly became moist and the bacilli gathered in them.

Dr. J. McGrath said there seemed to him to be a misconception about the definition of sepsis. It was defined as being definitely produced by steptococci, but it should be more widely understood that streptococci were not the only cause of puerperal sepsis. Other organisms such as staphylococci and coliform organisms definitely caused sepsis. A swab should be taken from within the cervix and from within the uterus. The taking of a swab and the avoidance of contamination were extremely important points. He had recently swabbed the cervices of a number of women who were almost normal and a number of them had haemolytic streptococci, although there was hardly anything wrong with the patients. So the finding of streptococci in the cervix did not necessarily show that puerperal infection was present. It should be remembered that streptococci fell into various

classes, and only some of the haemolytic streptococci found in throats and in cervices were really dangerous. In order to find out which were dangerous certain expensive sugar examinations had to be carried out. Even streptococci which were pathogenic had further to be divided serologically. Damp masks were a source of danger. He thought that cellophane masks only diverted the current of air and were not really efficacious in preventing infection.

Dr. BETHEL SOLOMONS said that he would first deal with the question of masks in relation to obstetrics and puerperal sepsis. During his seven years' mastership, when about 30,000 cases were delivered in connexion with the hospital, there was *no* outbreak of sepsis. It had been suggested that building operations predisposed to sepsis: during his mastership a new wing had been built. At the Rotunda Hospital lately when masks were not worn such an outbreak had occurred. At the Coombe Hospital where masks were worn there had been a similar outbreak.

It had been definitely proved that a large number of people were carriers of virulent haemolytic streptococci in their respiratory passages: he agreed with the Master of the Rotunda Hospital that he could not continue to avoid the use of masks. Dr. Solomons emphasized the fact that it must be taught that throat infection was one of the rare causes of puerperal sepsis. Sepsis should be treatel by preventive means and especially by the teaching of good obstetrics and by the avoidance of meddlesome midwifery.

If masks were worn there should be a layer of cellophane between the layers of gauze; this prevented the occurrence of moisture. He had used cellophane for many years in operative work. He did not think the experience of getting nurses to shout "bear down" over agar plates were useful: there was bound to be a growth. Nurses and students should be taught not to talk over the genitalia. If there was strict supervision about this there would be no droplet infection. He believed that small isolation wards were essential.

He had always taught that puerperal sepsis consisted of a group of diseases and that it depended on the ability of the accoucheur to find the correct treatment for the individual cases in order to obtain cures.

Mild cases would be cured by any drugs and this accounted for the variety of drugs suggested and cures achieved by different methods. Severe cases required meticulous care in diagnosis. Surgery had an extremely small place, but it had a place. He was sorry to hear that intra-uterine douches were still given in the Coombe Hospital. Drainage by tube was safer. He was surprised that quinine had not been mentioned, it was useful orally, intramuscularly and intravenously.

Dr. W. P. O'CALLAGHAN asked if any effort had been made in the Rotunda Hospital to group streptococci haemolytically. The fact that a patient had no fever did not show that there were no haemolytic streptococci present. In Holles Street Hospital they had found the routine swabbing of septic throats of considerable value in reducing the rate of sepsis.

Dr. W. H. ASHMORE showed two masks which he had invented. He said he was convinced that although endogenous infection might occur, nurses

with septic teeth or septic tonsils were the principal cause of sepsis. Nurses did not realize the danger of carrying on a conversation during parturition. He was quite sure that apart from a few cases of endogenous infection, droplet infection from an infected throat was the great source of infection. He hoped that the day would come when a doctor or a midwife would not attend a case of labour without wearing a mask.

Dr. ALAN THOMPSON said that in the old days infection was supposed to come through the genital passages. Nowadays the most likely route of infection was from the woman's own throat, and he thought that this fact was rather well borne out by the epidemic in the Rotunda Hospital. A probable mode of infection in some cases was an intermittent invasion of bacteria in the blood-stream, which infected the uterus and the breasts. He would suggest the routine swabbling of women's throats while they were waiting for their confinements, and, if haemolytic streptococci were found, means might be adopted to get rid of them or to check them until the puerperium was over.

Dr. T. O. GRAHAM said he did not know how to disinfect a throat which was infected with haemolytic streptococci. If the tonsils were badly infected he enucleated them. By aspiration it was possible to get rid of some of the pus from the crypts, but the crypts were very deep and so it was impossible to get all the pus out. He found that 25 per cent of his patients had haemolytic streptococci in their throats, and was of opinion that 25 per cent of the normal population had. He swabbed his patients' throats with paint and gave them a gargle, but there was nothing else to be done. Haemolytic polyvalent anti-streptococcal serum was quite useless and dangerous too, as he thought that by using it one was probably doing something harmful. He had found it perfectly useless on every occasion on which he had used it. The only anti-toxin which was of any use was scarlatinal anti-toxin. He mentioned two cases of septicaemia in which he had given this, both of which had recovered. If pus formed in a case of septicaemia, the patient would probably recover. If a fixation abscess occurred it was all to the good, and exceedingly helpful. He had long since given up using collosol iodine. He was not satisfied that iodine was an intravenous bactericide. He had found prontosil very efficacious.

The President said that it was interesting to note that there had been an outbreak of infection in a hospital where masks were not worn, and another in a hospital where they were worn. It was very foolish to say if masks were worn puerperal sepsis would not occur, and it was equally foolish dogmatically to say that masks should not be worn. Masks should not have less than four layers of gauze, and should be changed frequently. The principal thing about the wearing of masks was that the nurses should be watched to see that they did not handle the masks once they had been put on. The only cure for puerperal sepsis was to prevent it, and the first way of doing this was to make sure that the people in the hospital were free from infection. In Holles Street Hospital, of which he was master, before a nurse was allowed to go into the labour ward a swab was taken from her throat and if it was found to contain haemolytic streptococci she was not

allowed to go on duty. Every nurse's throat was sprayed every day. There was, of course, always the danger of infection occurring in a ward itself. Infection through the air sometimes occurred. There should not be such a thing as an isolation ward; infected patients should be in single rooms. The place of surgery in puerperal sepsis was very limited, but there was a small place for it. He thought that in some cases exploration of the uterus was definitely indicated. This was one of the reasons why he thought it was wrong to send cases of puerperal sepsis to a fever hospital. These cases were obstetrical, and should be kept in separate rooms, or if these were not available in an isolation ward in a maternity hospital. He did not think that serum was of any use unless it was given prophylactically or in the very early stages.

Dr. DAVIDSON, in replying, said that the real thing about masks was that they should be changed frequently. He had operated for years with masks made of only a single layer of gauze. Masks should be simply made, destroyed after use, and changed frequently. In most cases he used at least 150 cubic centimetres of anti-scarlatinal serum. Anti-streptococcal serum was of no use at all. He had the greatest possible belief in glycerine, and thought that it drained the uterus in these cases in a better and safer way than anything else. He did not believe in collosol iodine.

Dr. R. M. CORBET, in replying, said that he looked on intra-uterine douching in puerperal sepsis in general as an extremely dangerous weapon, but in some cases it was very useful. He was not advocating douching except in this particular type of case. Eight days was a very short time to keep patients in hospital. In the Coombe Hospital they tried to keep them for nine days. But the patients were always so anxious to get home that sometimes they would not even stay for eight days. If cases were kept for only eight days instead of nine, it was possible approximately to handle 100 more deliveries in the year. He thought that in many cases the good results of prophylactic serum were due to the fact that it was given to patients who were not going to develop sepsis.

Dr. J. S. QUIN, in replying, referred to the length of time in cured cases in which the streptococcus lay dormant, and said that he had recently had a patient under his care who had had a steptococcal infection 18 years previously.

Dr. DOYLE replied, and the meeting concluded.

A Meeting of the Section of Obstetrics of the Royal Academy of Medicine in Ireland was held in the Royal College of Physicians on Friday, November 20th, 1936.

Dr. NINIAN FALKINER, in the absence of the President, was in the chair.

Dr. BETHEL SOLOMONS showed

A GRANULOSA-CELL TUMOUR OF THE OVARY

which he had removed at Steevens' Hospital.

The patient was 30 years of age and consulted him because of amenorrhoea from which she had suffered for 11 months. She also complained of sterility.

The pelvis was normal. Following a short course of luteinizing and substitution therapy she menstruated twice, after which she again suffered from amenorrhoea for about seven weeks, when she returned complaining of haemorrhage and acute pain in the right side. An adnexal swelling about the size of a turkey's egg was discovered, and, as a possible diagnosis was ectopic gestation, she was admitted to hospital; the tumour and the appendix were removed.

On microscopic examination the growth proved to be a typical granulosa-cell tumour.

Dr. BETHEL SOLOMONS dwelt on the rarity of these tumours and said this was the first reported to the Royal Academy of Medicine in Ireland.

He quoted the figures of Schiller, Lepper, Baker and Vaux, and mentioned that the first case was reported in 1895 by Van Kahlden.

An interesting point about this case was that there was no sign of the tumour until the hormonic treatment was started, and he raised the question whether the treatment caused the growth or stimulated a tumour already present. It will be interesting to follow up the case to note if the menstrual function will become normal after the removal of the tumour.

Dr. NINIAN FALKINER said that this was the first case of granulosa-cell tumour which had been reported at the Academy. He had been of opinion that these growths were more often found in women at, or near, or past the menopause, and that one of the outstanding symptoms was the onset of severe haemorrhage after a period of amenorrhoea. He had on a previous occasion pointed out that the giving of antuitrin S was open to some criticism because it was related to the carcinogenic substances, and he was of opinion that in this case there was a relation between the giving of antuitrin S and the growth of the tumour.

Dr. GERALD DOCKERAY said he had previously seen this tumour and also the sections, and the sections seemed to him to be very typical of a fully matured granulosa-cell tumour. It was interesting to note that the trabeculae were formed *in situ* and were not due to any invasion of the follicles by trabeculae. These cells were not specific for granulosa-cell tumours as they had been found in carcinoma in mice. He had no doubt that this tumour was benign. When these tumours became malignant they were usually bilateral. In a granulosa-cell tumour columnar epithelioma was never found, and even in cases which were supposed to be malignant there was always a doubt whether they really were granulosa-cell tumours or not. About 42 per cent of these cases occurred at the climacteric, about 40 per cent at puberty, and the rest at any period. In some of the younger patients these tumours had produced amenorrhoea. It was interesting to note that the amenorrhoea was not due to an excess of folliculin or to lack of it. Three of these tumours, out of 16 reported by Dr Schiller, had shown evidence of virilism.

Dr. J. MCGRATH said he agreed that this was a giant-cell tumour. His only experience of these cases was through contact with Dr. Schiller and through some slides which Dr. Schiller had given him. He thought that this case was definitely not malignant. It was curious that when one got a knowledge of tumours which appeared to be rare they turned up when

perhaps they had been missed before. He had seen a granulosa-cell tumour a little time ago which had been removed. It was about twice the size of the one shown by Dr. Solomons. It had a superficial resemblance to the microscopical appearance of a rodent ulcer.

Dr. F. DOYLE, referring to the masculine distribution of hair in this patient, said that these tumours were supposed to have a hormonic basis which was particularly to be seen in relation to the secondary sexual characters.

Dr. F. S. BOURKE said that when he had first seen this tumour he thought it was a carcinoma of the ovary. From the rarity of granulosa-cell tumours he thought that this was a pardonable error. Looking at the tumour with the naked eye one would not imagine that such a smooth surface would belong to a granulosa-cell tumour. He did not think that folliculin could produce a masculine distribution of hair.

Dr. BETHEL SOLOMONS in reply said that his patient was 30 years of age. Schiller's figures as to age incidence showed that 42 per cent occurred about the menopause.

The question of malignancy was important and as this growth was not malignant further investigation was not necessary. The woman said she might have had a miscarriage five years previously.

Dr. R. M. CORBET showed a specimen of

KRUKENBERG'S TUMOUR, SECONDARY TO CARCINOMA OF THE STOMACH.

This patient had originally been admitted to the Coombe Hospital with a diagnosis of hyperemesis gravidarum. However, an X-ray photograph of the gastro-intestinal tract showed a tumour at the pyloric end of the stomach. Labour was induced and partial gastrectomy was performed in the Mater Hospital. Eighteen months later, the patient was re-admitted with an abdominal tumour the size of a five months' pregnancy, and this proved to be a large Krukenberg's tumour of the right ovary with a small tumour of the left ovary. Microscopic slides and lantern slides from microphotographs, which were very beautifully made by Dr. McGrath of Vincent's Hospital Pathological Department, were shown. These showed the typical features of the Krukenberg tumour, large numbers of signet ring cells being observed.

Dr. J. MCGRATH said that about three years ago he had seen a tumour similar to the one shown by Dr. Corbet. It was a double tumour of the ovary. The ovaries were each about as big as a fist. A short time after operation the patient died, and at post-mortem examination a leather bottle carcinoma of the stomach was found. He had also seen a case in which a dermoid cyst had been quite hidden by the tumour. In this case one ovary contained a very large tumour, and the other a very small one. The slides had shown stroma through which was a mass of fibrous tissue, and the cells had shown a signet ring appearance.

Dr. NINIAN FALKINER said he was interested to note that this case had been admitted to hospital as a case of hyperemesis in which the vomiting was due to a pre-existing condition. This was a reminder that such conditions

should not be overlooked in cases of hyperemesis gravidarum. He had seen one case in which the diagnosis had not been made during life, but at autopsy two tumours had been found in the pelvis, not as large as the tumours in the present case. It was difficult to understand why an ovary should be the site of a malignant growth if it was due lymphatic spread. The prognosis in these cases was, he thought, always bad. There must be some relation between growths in the ovary and growths in the intestinal tract.

Dr. GERALD DOCKERAY said he had no doubt that this was a Krukenberg tumour although it was not quite the same as a few Krukenberg slides which he had recently seen. But it contained the signet ring cells, although they were not the most obvious part of it. This specimen was more like the picture of Krukenberg's tumour in Dr. Teacher's book, in which the primary carcinoma was in the breast. He had no doubt that in the past some granulosa-cell tumours had been reported as Krukenberg's tumours, and these would be reported as Krukenberg's tumours which had been operated on and the patients recovered.

Dr. D. J. CANNON asked if the uterus had been removed in this case.

Professor FRANKLN took the view that these cases were undoubtedly due to lymphatic spread, and this had been demonstrated in Budapest, where carcinoma had been found in the lymphatic nodules.

Dr. CORBET, in replying, said that this condition had first been described 40 years ago. The chief argument in favour of lymphatic spread was the finding of tumour cells actually in the lymphatics. To his mind the fact that the tumour seemed to grow from the inside of the ovary and not from the outside was in favour of lymphatic spread. The fact that the surfaces were so smooth was in favour of the condition's not being a transperitoneal implantation. One case was reported in which the patient was alive three years after the removal of the tumours. The uterus was not removed in his case. It was quite small and hard, below and behind the tumours. When the abdomen was opened there was no doubt at all that the case was one of Krukenberg's tumour. The peculiar thing was that one tumour was so much larger than the other. The large tumour was quite free, but the small one was adherent to the wall of the pelvis. These tumours had originally been described as having the features of a fibro-sarcoma, and these features had never been entirely explained.

Dr. MCGRATH, in replying, said that the cells did not contain any fat, and were spread round the central area of the secretion.

Dr. T. M. HEALY described his

EXPERIENCE OF HALBAN'S OPERATION, FIRST PUBLISHED IN 1922, FOR CLOSURE OF THE FIMBRIATED END OF THE FALLOPIAN TUBE.

The original technique was simple division of a functioning part of the Fallopian tube, between two catgut ligatures. Dr. Healy had used a single silk ligature on each tube, without cutting the tube at all. In some cases he tied the mesosalpinx distal to the ligature on the tube. He had used this technique in 11 cases of primary sterility. Two patients had subsequently been delivered of living children. One had become pregnant after an interval of six months, and the other after three years. He had carried out Rubin's

test on six of the remaining nine cases, and found the Fallopian tubes patent in one case. He stated that the method was on trial, and that no conclusions should be drawn from a small series of cases.

The Master of the Rotunda Hospital (Dr. A. H. DAVIDSON) said that this procedure seemed to be an extraordinarily simple way of dealing with a very definite problem, and the results which Dr. Healy had obtained seemed to be sufficiently successful to warrant the adoption of the method. He asked Dr. Healy if he had had successful results in cases in which the block was near the uterine end of the tube. He had at one time spent a great deal of time working on Fallopian tubes in endeavouring to cure sterility and had obtained only one cure and two cases of ectopic gestation. He had had success in cases in which he had tied the tube towards the inner end and in which the outer end had been destroyed by a block. He thought he might have been more successful if he had tried to make a cuff, leaving the Fallopian tubes open, and not tying them. He had seen Professor Young sterilize a patient with tuberculosis by performing hysterotomy, taking the tube and making a knuckle of it, tying a ligature round it and cutting off the knuckle. Professor Young said that this method of tying the tube was the most successful in preventing pregnancy.

THE MASTER OF THE COOMBE HOSPITAL mentioned a case which he had recently seen; the patient had been sterilized on three separate occasions after Caesarean section. She had a contracted pelvis.

Dr. NINIAN FALKINER said he was struck by the good results of the operation described by Dr. Healy and by the considerable percentage out of a small number of cases which had become pregnant. He asked Dr. Healy if in cases of sterility, which afterwards had Caesarean section, he found that the whole lumen of the Fallopian tube was open, or if the tube had a new lumen such as one would expect to follow the technique which he adopted.

Dr. BETHEL SOLOMONS said on the rare occasions when patients were sterilized he removed a knuckle of the Fallopian tube; pregnancy had never followed.

Dr. Healy's cases all dealt with sterility due to blockage at the fimbriated end of the Fallopian tube and two successful cases in 11 were what one could, at least, expect when the block occurred in that situation. The simplicity of this procedure was noteworthy. Experimental work on the Fallopian tubes of animals was not satisfactory and gynaecologists should persist in endeavouring to find a solution to the problem of tubal sterility.

Dr. HEALY, in replying, said that in any cases of Caesarean section which he had seen the Fallopian tube had been amputated by the ligature, and he could not see any reason why the part of the tube distal to the ligature should disappear. There was merely a stump of tube left and a new ostium had formed; the general appearance of the end of the tube was as if it was meant to be like this. His experience was limited to ligature of the ampullary portion of the tube. It was normal for the tube, during ovulation, to grasp the ripening follicle which was about to burst, and this was probably the reason why operations near the uterine end of the tube were not usually successful.

Dr. EDWARD SOLOMONS read a communication on

INTRAVENOUS ANAESTHESIA IN OBSTETRICS.

He gave a short resumé of the history of the subject, and the various anaesthetics used both by inhalation and intravenously; he indicated the disadvantages of the several preparations. He then described a series of 46 cases in which he had used pentethal as an anaesthetic in labour. He said this substance detoxicated more rapidly than evipan and got over the trouble of twitching and movements which sometimes occur during the induction period with the latter drug. It had no effect on the baby in any of his cases. It was apparently safe and it could be used after scopolamine and morphia had been administered.

He referred to work done in America and on the Continent with this drug, where considerable series of cases without a death had been published.

Dr. NINIAN FALKINER said that the use of a safe intravenous anaesthetic for delivery and other procedures was a tremendous boon for a person who could not get a competent anaesthetist, but he thought an anaesthetist should always be present, if possible, when the anaesthetic was a substance such as pentethal which could be given intravenously. He thought it had been proved that the barbiturates did enter the foetal circulation when the concentration reached a certain level in the maternal blood. He had on one occasion given nembutal intravenously early in labour and the foetus suffered from asphyxia when it was born and could not be revived, so he had not given nembutal since then.

Dr. G. P. MELDON said he had not used pentethal but he had had a good deal of experience with intravenous injections. He thought that intravenous medication with barbiturates was very much more simple than giving them by mouth.

Dr. TIGHE drew attention to the fact that Dr. Solomons was the first person in Dublin to use pentethal. He had used evipan for some time and had found it satisfactory except that sometimes muscular movements occurred which at times were rather alarming. He asked Dr. Solomons if he had tried pentethal in a case of normal labour, and said he thought it was easy enough, no matter what form of anaesthesia was used, to give the patient relief at the actual time of delivery, but that what was wanted was some drug which could be used in small amounts over a long period of time.

Dr. R. W. SHAW said that he had used pentethal for some months, but had not used it in nearly so many cases as Dr. Solomons had. He had been using the barbiturates for some time and had not found that they gave rise to any anxiety. He did not think, however, that they should be used in conjunction with any other hypnotic, nor should they be used following the oral administration of any barbiturate. He always used them alone, never in conjunction with any other barbiturate. The chief contra-indication to their use was hepatic derangement. They should never be given to alcoholics or to people who were being treated with neosalvarsan. For excessive depression of respiration he gave pure carbon dioxide followed by coramine. He was glad to notice that Dr. Solomons did not think that the barbiturates

had any effect on the foetus. On two occasions he had given nembutal for Caesarean section, and on each occasion the baby was rather blue and the nembutal was blamed for it. An anaesthetist should be very careful what drug he uses. He was always more anxious about a patient to whom he had given a barbiturate, or a spinal injection, because there was always the possibility that if anything went wrong the surgeon might say that if the barbiturate, or the spinal anaesthetic, had not been given nothing would have gone wrong.

Dr. J. BECKETT said he thought Dr. Solomons had shown great pluck in using intravenous anaesthesia in obstetric work and in being the first person in Dublin to use pentethal. He was always rather afraid of the effect the barbiturates might have on the foetus. He thought it was a mistake to give any drug before an intravenous anaesthetic.

Dr. T. M. HEALY asked if Dr. Solomons had had any trouble with his patients in the recovery stage following the various procedures which he had carried out. He had seen patients as long as eight hours after the injection of nembutal behaving in a very irresponsible way.

Dr. R. M. CORBET said he was not in favour of intravenous anaesthesia. It seemed to him impossible that such a very powerful drug, which would produce complete anaesthesia in a matter of seconds, could be free from grave risk. Pentethal was a drug which had been used almost entirely in conditions which inherently had an exceedingly low mortality, and in using it he thought that a drug was being used which had a very definite mortality, a mortality considerably higher than the operations for which it was used. He thought it was the job of an anaesthetist to give whatever drug was used, rather than that of the operator.

Dr. A. W. SPAIN said he had never used evipan because he was nervous of it. He thought it was a dangerous drug generally to recommend for obstetric cases because it was supposed to be dangerous for anyone who had toxaemia, and it was very easy in obstetric cases to miss patients having some forms of toxaemia. When there was any contra-indication to the use of evipan it appeared to be very fatal. He thought it was wise to proceed very slowly with the use of intravenous drugs in obstetrics.

Dr. VICTOR MCCORMICK said he was against the use of evipan. He had seen some deaths following its administration, and they had nearly all been in cases in which the patient should not have died. It was impossible to do big work with evipan, and fatal results should not follow in cases of minor surgery. He had seen one fatal case following the administration of evipan in which there had been no previous medication at all. He thought it was due to too large a dose over a long period of time. An anaesthetic which was really good should have a death-rate of one in 10,000. He did not think that any of the barbiturates had a rate so low as this.

The Master of the Rotunda Hospital said he thought there were two questions to ask when using the barbiturate drugs: " Is the patient alive? " and " Is the baby alive? " In all the cases in the Rotunda Hospital in which pentethal had been used both mother and baby were alive. The nurses in the hospital did not like giving either soneryl or nembutal. He

had had two frights in private practice following the oral administration of nembutal and had decided not to use it again. Too small a number of cases had yet been treated to pass any real comment on pentethal, but it was very handy to use in cases in which an anaesthetist was not on the spot. He thought that a drug should be shown to be as free from risk as ether before it was generally introduced into hospital use. Chloroform had not been used for a number of years in the Rotunda Hospital; ether had been used.

Dr. F. DOYLE said he thought some research on anaesthetics was necessary. It was only when they were properly put to the test that it was possible to assess them at their true value. He had gone a good deal into the question of anaesthetics, and after trying many methods, had come to the conclusion that the one and only anaesthetic to produce analgesia, as well as anaesthesia, was nitrous oxide. In Berlin he had recently seen continuous evipan being given. He had seen Wertheim's hysterectomy done under it, and had been greatly impressed with the results he had seen following its administration. In Berlin it was given in conjunction with saline. It was also being used extensively in Budapest, and there was no doubt that in proper hands it could give extremely good results. It was very dangerous to give morphine or anything of that nature in conjunction with the barbiturates.

Dr. SOLOMONS, in replying, said that he thought it was very important to have a drug which could be used in a private house. He thought that chloroform *ad libitum* was much more dangerous than pentethal. Undoubtedly the barbiturates must to a certain degree enter the foetal circulation, but babies seemed to show very little effect of that. It was necessary to have experience in giving intravenous medication, as it was not always at all easy to introduce a needle into the vein. If pentethal leaked into the tissues round the vein it was stated not to have any more effect than saline. Dr. Herbert's cases had all been given either omnipon or scopolamine before pentethal, if the operation was going to be a big one. In pre-medication it was necessary to know exactly what was being given. Some patients to whom he had given nembutal and also evipan had become very restless and had had to be watched very carefully, but this had not occurred in any of the patients to whom he had given pentethal. It was excreted much more rapidly than any of the other barbiturates. A patient with any degree of toxaemia should not be given pentethal. The cases should all be carefully selected, and it was necessary to have a very full knowledge of the patients. He thought that pentethal was much safer than evipan. The cost was two shillings an ampoule, and frequently it was possible to use one ampoule for two patients, so it was not very expensive. There were, of course, bound to be patients with idiosyncracies to every type of drug, but as long as pentethal was carefully given and cases were carefully selected there was little risk.